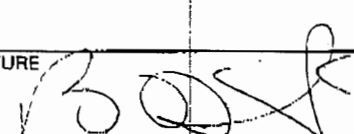# Synthesis, Evaluation, and Formulation Studies on New Oxidizers as Alternatives to Ammonium Perchlorate in DoD Missile Propulsion Applications

SERDP Project WP1403
Final Report

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Acronym List

ABL – Allegheny Ballistic Laboratory

ADME – absorption-distribution-metabolism-excretion

ADN – Ammonium Dinitramide

ADNA – Ammonium di(nitramido) amine

ADNDNE – diammonium di(nitramido) dinitoethylene

AN – Ammonium Nitrate

AP – Ammonium Perchlorate

ATK – Alliant Techsystems

BDNPA/F – bis(2,2-Dinitrpropyl)acetal/formal nitroplasticizer

Boc –t-butoxycarbonyl

CL-20 – hexanitrohexaazaisowurtzitane

Del-Isp° - Delivered Isp° (Actually produced in motor not predicted)

Del-Den-Isp° - Delivered Den-Isp° (Actually produced in motor not predicted)

Den-Isp° - Denisty and Isp° product.

DGTN – diglycerol trinitrate

DMAP – dimethylaminopyridine

DMF – dimethylformamide

DNNC – 1,3,5,5-tetranitrohexahydropyrimidine

DSC – Differential scanning calorimetry

DWEL – Drinking Water Equivalent Level

EPA – Environmental Protection Agency

ESD – electrostatic discharge

FOX-7 – 1,1-diamino-2,2-dinitroethene

GAP-P – glycidyl azide polymer – plasticizer (nonfunctional)

GO – positive test result

HAN – hydroxyl ammonium nitrate

HCO – 1,3,3,5,7,7-hexanitro-1,5-diazacyclooctane

HMX – octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine

HNF – hydrazinium nitroformate

ips – inches per second (linear burn rate)

Isp° - Specific Impulse, standard condition (1000 psi expanded to 14.7 psi)

K_{OW} – Octanol/water partition equilibrium constant

NC – Nitrocellulose

NG – Nitroglycerin

NO GO – negative test result

NOL – Naval Ordnance Laboratories

NR – no reaction

Obal – Oxygen balance = ((moles oxygen) – (2 moles carbon + ½ moles hydrogen + 1.5 moles aluminum))

OCAL – moles oxygen/(moles carbon + 1.5 moles aluminum)

O/F – oxidizers to fuel ratio

ppb – Parts per billion

QSAR – quantitative structure-activity relationship

RDX – hexahydro-1,3,5-trinitro-1,3,5-triazine

RfD – reference dose

PGN – polyglycidyl nitrate

Pl/Po – ratio of plasticizer weight and combined polymer and curative weight

SBAT – Simulated Bulk Autoignition Temperature

TC – Thiokol Corporation

TFAA – Trifluoroacetic acid

THF – tetrahydrofuran

TMSOTf – trimethylsilyl triflate

1 EXECUTIVE SUMMARY

Perchlorate is found in groundwater and drinking water throughout the United States. This contamination is primarily attributed to the use of ammonium perchlorate in the solid fuel for rockets and missiles. The concern with perchlorate is that it competes with iodine for uptake into the thyroid gland. This can result in an iodine deficiency. There is considerable debate on what is a proper oral reference dose for perchlorate. The Department of Defense must concern itself with the standards adopted by the EPA for perchlorate in groundwater. While the debate is not complete, a perchlorate drinking water equivalent level (DWEL) of 1 ppb is proposed in the EPA draft document released January 2002.

The objective of the program is to develop environmentally benign solid rocket propellant formulations that do not rely on the use of ammonium perchlorate (AP) as an oxidizer. This objective supports the goal of reducing future AP contamination in groundwater by reducing the need for production and use of AP as an oxidizer in solid rocket motors. The propellants developed must match current performance and hazards to meet the objective.

To formulate propellants that don't rely on AP, combinations of oxidizers must be exploited. Several oxidizers are compared in **Table 4—1** below. ATK Launch Systems Group has made stable composite propellants using ball powder (60/40 NC/NG) in combination with plasticizers that don't swell the NC. The ball powder system (NC/NG) is low cost, and sensitive to ballistic modifiers such as bismuth compounds. Thus, we used ball power with a supplemental oxidizer to replace AP on this program.

We selected four new supplemental oxidizers to focus on initially. These include the inorganic oxidizer ammonium di(nitramido) amine (**ADNA**); the cyclic nitramine/gem-dinitro compounds such as 1,3,5,5-tetranitrohexahydropyrimidine (**DNNC**) and 1,3,3,5,7,7-hexanitro-1,5-diazacyclooctane (**HCO**) and by adding the dinitroethylene attachment to nitramide functions as seen in diammonium di(nitramido) dinitroethylene (**ADNDNE**). These compounds are shown below in **Figure 4—1**.

Extensive attempts to synthesize ADNDNE were unsuccessful. No ADNDNE was produced. The extra time spent on ADNDNE resulted in no effort being spent on ADNA. The intermediates for HCO were too hazardous to make scale up feasible. A small amount of HCO was made but new synthetic methods will be needed for scale up. DNNC was produced at the 25 gram scale. Scale up of DNNC was in progress when other technical issues caused the program to be terminated.

AMEC Earth & Environmental (AMEC) conducted a screening level assessment of the fate, transport, and toxicity of four potential replacements for perchlorate. The data derived from this project will be helpful in evaluating and minimizing potential environmental liability associated with the use of energetic compounds as propellants.

The compounds evaluated in this screening level assessment include the inorganic oxidizer ammonium di (nitramido) amine (ADNA); the cyclic nitramine/gem-dinitro compound 1,3,5,5-tetranitrohexahydropyrimidine (DNNC); 1,3,3,5,7,7-hexanitro-1,5-diazacyclooctane (HCO); and diammonium di(nitramido) dinitroethylene (ADNDNE). In addition to these, AMEC evaluated the following analogue compounds that are currently in use: ammonium dinitramide (ADN) as an analogue for ADNA; hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX) as an analogue for DNNC; octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX) as an analogue for HCO; and

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1,1-diamino-2,2-dinitroethene (FOX-7) as an analogue for ADNDNE. Finally, ammonium perchlorate was evaluated as the basis for comparison.

The four compounds in **Figure 4—1** are predicted to have a low lipophilic nature as shown by low predicted log K_{ow} coefficients. This favors migration to surface water or ground water but also indicates these compounds would not bioconcentrate into aquatic organisms or biomagnify within the food chain. Direct toxicity to aquatic organisms is also predicted to be very low.

Compared to AP, the compounds are anticipated to behave similarly from an environmental fate and transport perspective. However, each of the compounds, are either much less soluble in water than AP or are expected to adsorb onto clay and soil better or will readily photodegrade. It is reasonable that each of these four compounds would be an improvement over AP for fate and transport. The compounds are ranked currently DNNC, ADNA, HCO, ADNDNE according to the method described.

Propellant formulation data were collected. First, a propellant trade study revealed propellant formulations using ball powder and supplemental oxidizers replacing AP that can meet the performance goals of the program. Initial formulation characterization was completed on the Ball powder/CL-20 example. The testing revealed shock sensitivity much greater than anticipated. CL-20 is a commercially available high density energetic material and was used for initial characterization due to the delays in synthesizing the new oxidizers discussed above.

The formulation made gave a GO result in the Large Scale Gap Test at 120 cards. A Hazard Class 1.3 propellant would be expected to be a NO GO at 70 cards in the test. State of the art Class 1.1 formulations have NO GO values about 130 cards in this test, but have more performance. The amount of supplemental oxidizer used is small (<13%) so even if other supplemental oxidizers have lower shock sensitivity than CL-20, it would not be enough to make a difference.

Thus the technology developed on this program to replace AP results in propellant formulations that have Class 1.3 performance with Class 1.1 hazard properties. Since Class 1.3 is a requirement, it does not appear practical to use this technology to replace AP.

2   OBJECTIVE

The objective of the program is to develop environmentally benign solid rocket propellant formulations that do not rely on the use of ammonium perchlorate (AP) as an oxidizer. This objective supports the goal of reducing future AP contamination in groundwater by reducing the need for production and use of AP as an oxidizer in solid rocket motors. The propellants developed must match current performance and hazards to meet the objective. Thus a delivered-Isp° (del-Isp°) of 248 sec (at 1000 psi expanded to 14.7 psi) with a delivered-density-Isp° (del-den-Isp°) of 16.2 sec-lb$_m$/in^3 is required. Also, formulations with a modifiable burn rate that can achieve low burn rates (ca. 0.3 ips at 1000 psi) and a pressure exponent less than 0.5 will be pursued.

3   BACKGROUND

Perchlorate is found in groundwater and drinking water throughout the United States. This contamination is primarily attributed to the use of ammonium perchlorate in the solid fuel for rockets and missiles. The concern with perchlorate is that it competes with iodine for uptake into

the thyroid gland. This can result in an iodine deficiency. There is considerable debate on what is a proper oral reference dose for perchlorate which is expressed in mg (perchlorate)/kg (body weight)-day. The industry must concern itself with the standards adopted by the EPA for perchlorate in groundwater. While the debate is not complete, a perchlorate drinking water equivalent level (DWEL) of 1 ppb corresponding to an oral reference dose (RfD) of 0.0003 mg/kg-day is proposed in the EPA draft document released January 2002.

It has been estimated that more than 24 million pounds of AP is produced each year. The industry must concern itself with the standards adopted by the EPA for perchlorate in groundwater. If groundwater contamination by ammonium perchlorate must be reduced or eliminated, then the use of AP in solid rockets will have to be reduced or eliminated. Under this scenario, environmentally benign solid rocket motor technologies that do not rely on AP will be needed. This program was designed to develop propellant technologies, which yield high performance propellants that are Hazard Class 1.3, and have a modifiable burn rate.

4 TECHNICAL APPROACH

The selection of new oxidizer molecules that can replace AP is a challenge. The perchlorate anion is a high-density source of oxygen atoms. The cluster of four oxygen atoms around a central chlorine atom is an efficient and stable arrangement that can, given sufficient ignition impetus, transfer oxygen to a fuel for a net energy gain during combustion. A similar cluster of oxygen about a central atom that would replace the perchlorate anion does not appear feasible.

Many programs and patents have explored the feasibility of replacing AP with non-halogenated oxidizers (e.g. HNF, AN, ADN, HAN). All of these present significant problems in performance, sensitivity, toxicity or stability. It is difficult to conceive a single practical compound that could replace AP. However, it is reasonable to envision AP free propellants with the same performance characteristics with the application of a judicious combination of environmentally friendly organic and inorganic fuels and oxidizers. One promising approach is an extended anion with oxygen atoms on a nitrogen framework that can achieve stabilization as in the oxynitrogen anion, $N_3O_4^-$. The nitramide ammonium salt, ADN, first discovered in Russia and then independently in the U.S[1], is still being evaluated as an oxidizer in propellant formulations. It appears, however, to be susceptible to a slow decomposition at temperatures below its melting point. Given the properties of this compound, there is promise that a more extended nitrogen framework, with its more effective delocalization of charge, will provide an oxynitrogen anion with adequate stability characteristics.

Therefore, this program consisted of two concurrently running components. The first part was the synthesis of alternative high energy density, insensitive oxidizers. The second component of the program will be the formulation of these materials into propellants that meet the performance objectives. It would be very high risk and does not appear necessary to rely on the synthesis of excessively exotic ingredients in order to make propellants that meet the performance goals of this program.

4.1 NEW OXIDIZER SYNTHESIS

There are many potential oxidizer candidates that would need to be synthesized for use on this program. We selected four to focus on initially. These included the inorganic oxidizer ammonium di(nitramido) amine (**ADNA**); the cyclic nitramine/gem-dinitro compounds such as

1,3,5,5-tetranitrohexahydropyrimidine (**DNNC**) and 1,3,3,5,7,7-hexanitro-1,5-diazacyclooctane (**HCO**) and by adding the dinitroethylene attachment to nitramide functions as seen in diammonium di(nitramido) dinitroethylene (**ADNDNE**). These compounds are shown below in **Figure 4—1**.

The two nitramide salt structures, ADNA and ADNDNE, have the common feature that each provides two oxygen atoms for combustion, as is the case for AP. Each will have extensive delocalization of charge; one through a –N=N-NO$_2$ linkage, and the other through a –C=C(NO$_2$)$_2$ linkage. ADNA consists of an ammonium cation and a new oxynitrogen anion, with the composition of N$_5$O$_4^-$. This material would extend the charge found in the ADN anion, N$_3$O$_4^-$, over an additional two atoms. A higher melting point and greater thermal stability is anticipated. Due to the symmetry in the structure it might be anticipated that the bond orders due to de-localization will be equal, thus maximizing the stability of this anion. The estimated heat of formation of 43 Kcal/mol makes this oxidizer an excellent replacement for AP in terms of energy content.

A second option that is being proposed for an AP replacement utilizes a dinitroethylene attachment to the nitramide functions. This dianion, C$_2$N$_6$O$_8^-$, also provides two atoms of oxygen per molecule. In addition to allowing for extensive delocalization of the charges, the ethylene unit introduces more stability by separating nitrogen functionalities. The density of the diammonium salt is calculated to be 1.77 g/cc.
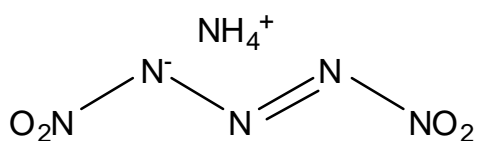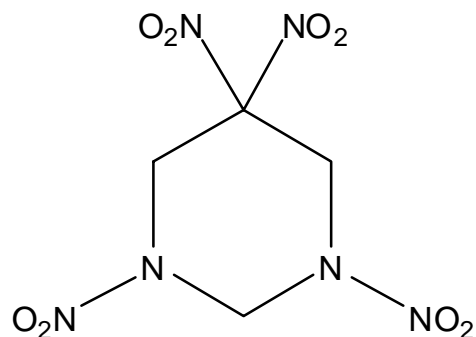
ADNA

ρ = 1.76 g/mL (calc)
ΔHf = +43 kcal/mole (calc)

DNNC

ρ = 1.82 g/mL
ΔHf = +11 kcal/mole
mp = 151-4 degrees C
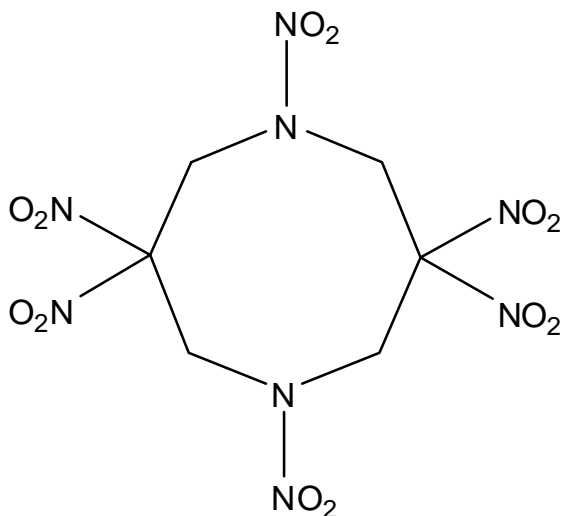
ρ = 1.875 g/mL
ΔHf = -6.52 kcal/mole
mp = 250 degrees C (dec)
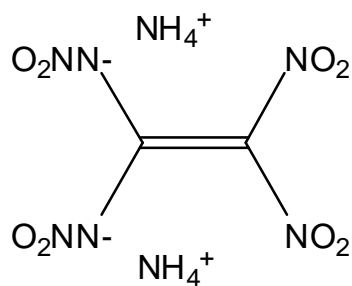
ρ = 1.77 g/mL (calc)
ΔHf = 4.02 kcal/mole (calc)

Figure 4—1. New Oxidizers for AP Replacement.

4.1.1 PROPOSED SYNTHESIS OF ADNA

For ADNA, there are various possible routes to assembling the nitrogen fragments of this anion. In analogy to a route that was carried out in this laboratory for the synthesis of ADN, a possible sequence would make use of nitrourethane to introduce the nitramide functions[2], and a silylated amine to couple with these to establish the central nitrogen **Figure 4—2**.
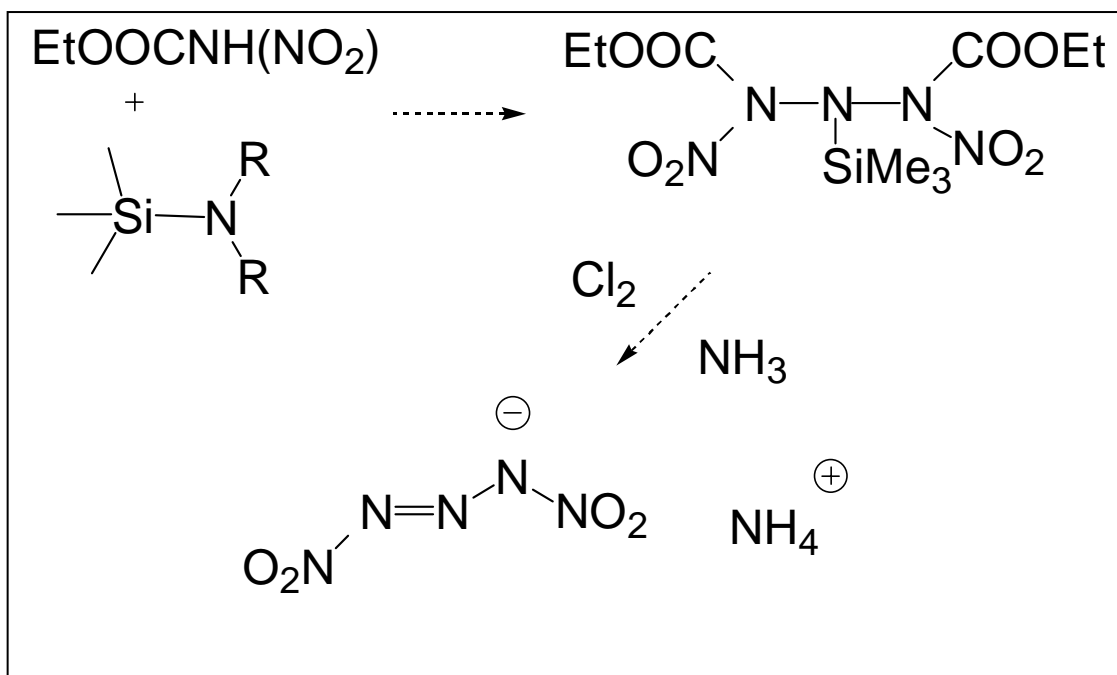
Figure 4—2. Proposed route to ADNA.

4.1.2 PROPOSED SYNTHESIS OF ADNDNE

A possible synthesis route to ADNDNE is through the known DADNE, diamino dinitroethlyene[3]. The reaction of oxalyl chloride with DADNE is anticipated to give the corresponding cyclic amide structure. Nitration and ammonolysis of the resulting cyclic nitramide should give the ADNDNE product.

With SERDP program manager concurrence the most attractive candidate materials were then to be made and tested in formulations. A team of chemists from ATK Launch Systems Group and NSWC Indian Head conducted the synthesis efforts. ATK focused on **DNNC** and **HCO**. NSWC IH Div focused on **ADNA** and **ADNDNE**.

4.1.3 PROPOSED SYNTHESES OF DNNC AND HCO

Both **DNNC** and **HCO** are known in the literature, and have been studied to some extent as potential oxidizers in propellant systems. The literature synthesis routes will be used to produce these compounds on the program with improvements developed as needed or as opportunities arise.

4.2   ENVIRONMENTAL SCREENING:

The objective of this part was to offer predictive estimates for the fate-and-transport and toxicological properties of new oxidizers proposed to replace perchlorate. It is desirable to assess whether the new oxidizers proposed to replace perchlorate are more or less "benign" than perchlorate from an environmental perspective.

Historically, the evaluation of success or failure of new oxidizers has focused on their performance as propellants, whereas little attention has been paid to the potential environmental liability. More recently, environmental mobility, persistence and potential toxicity issues related to perchlorate have raised the importance of trying to anticipate the environmental risk before beginning large-scale production of a new oxidizer. In other words, assessment of the environmental impact needs to be performed before embarking on an expensive synthesis effort. This task describes the use predictive methods in performing an up-front environmental assessment and providing information which is essential in the decision making process for selecting candidate perchlorate replacements.

The following is a plausible approach for assessing the fate, transport and aquatic toxicity of oxidizers early in their development. The approach presented is a phased- or tiered-approach that begins with simple, relatively low cost methodology: QSAR (quantitative structure-activity relationship) model estimation of the physicochemical and toxicological properties of a chemical. In this approach adequate data can be generated for all oxidizers in development so that they can be ranked in terms of their fate, transport, and toxic properties. Because the use of these oxidizers is typically limited to areas where access by the general public is precluded (i.e., military bases), exposure is primarily going to be determined by the chemicals propensity to disperse in the environment, i.e. to contaminate soil and quickly migrate to surface water or groundwater.

The activities conducted in the first year were as follows:

- The first step in the evaluation of the new oxidizers (4-6 candidate materials proposed herein) is to conduct a literature search to obtain any relevant information on fundamental properties that affect fate, transport, and toxicity.

- If data on the primary oxidizer is not available, a literature search will be conducted for surrogate chemicals (i.e., chemicals that have similar chemical structures and may behave similar to the oxidizer being considered).

- The second step involves conducting an initial screening and ranking using selected environmental software QSAR models (e.g., EPIWIN, ECOSAR) that predict physicochemical properties of a chemical, its disposition in various environmental media, and its subsequent toxicity should receptor exposure occur.

These models work by comparing the structure of the oxidizer in question to large chemical libraries containing thousands of similar compounds that already have known environmental properties. These properties are further regressed against known environmental behavior endpoints, such as persistence, bioaccumulation and toxicity. The model output provides a reasonably accurate assessment of how the chemical might partition to air, water, soil and sediment if it were to be introduced into the general environment. Some of the predictive output parameters include the octanol-water partition coefficient (K_{ow}), water solubility, Henry's Law Constant, propensity to biodegrade, half-life in air, soil adsorption coefficient, and half-life in

surface water. Those chemicals that rank lowest for potential environmental mobility and toxicity will be subject to fugacity modeling to estimate equilibrium concentrations in various environmental compartments (assuming a known flux to soil, air, water, sediment, and biota).

The data generated from the literature review and the QSAR modeling was used to rank the new compounds against perchlorate from a fate-and-transport/toxicology prospective. This data is discussed and a portion summarized in 5.2.1 and in **Table 5—4** and **Table 5—5**. The complete bibliography of 52 references and a list of public databases searched and the complete data is provided on pages 6, and 30-39 of section 8.1 which is the first Appendix to this report. The comparative ranking was limited to the data generated as part of the literature review and QSAR modeling. It's important to note that this screening-level analysis did not allow for a comparison of all physiochemical and toxicological properties that are known for perchlorate. For example, it is likely that studies of subtle chronic health effects of the proposed oxidizers will not be available, nor is this information generated as part of the proposed QSAR modeling. In contrast, data on subtle chronic health effects for perchlorate are available. As a result of the incomplete datasets, a comparison of chronic health effects will not be possible. Nevertheless, the data that are generated and used for the comparison are significant in their ability to assess the environmental viability of the proposed oxidizers with respect to perchlorate. A report was prepared at the end of Year 1 to summarize the predictive modeling assessment of the proposed oxidizers.

In the second and third year, uncertainties that remain from the predictive screening assessment were further evaluated. For the most promising compounds identified based on their oxidizer performance and fate-and-transport properties a predictive toxicology assessment was conducted using simplified absorption-distribution-metabolism-excretion (ADME) models. These models also work by comparing the oxidizer in question to the ADME of large datasets of similar compounds. Further assessment will be conducted on those oxidizers that are not amenable to using EPIWIN or ECOSAR. For example, most of these models may not be able to process oxidizers in the form of salts. Therefore, the oxidizers identified may have to be evaluated by transforming the polar molecule to a nonpolar surrogate (e.g., by covalent addition of a -H or -OH group). These nonpolar surrogates of the oxidizer salt will then be screened using EPIWIN and ECOSAR. The final predictive assessment might consist of simple batch scale tests such as the ability of the oxidizer to inhibit a p450 liver enzyme system, a biochemical oxygen demand test, a Microtoxic model, or any other type of *in vitro* test system. Reports were prepared in Year 2 summarizing the additional testing results.

It should be kept in mind that the assessments conducted in Year 1 are solely predictive based on the chemical structure of the oxidizers and the tests in Year 2 are only qualitative assessments. Further research would be needed, beyond that identified in this proposal, on the most promising oxidizers to quantify their fate-and-transport properties and potential for toxicity.

4.3   PROPELLANT FORMULATIONS

To formulate propellants that don't rely on AP, several oxidizers or combinations of oxidizers must be exploited. Oxidizers such as DNNC and HCO mentioned above have good oxygen balances (OBAL). Several oxidizers are compared in **Table 4—1** below. ATK Thiokol Propulsion has also made stable composite propellants using ball powder (60/40 NC/NG) in combination with plasticizers, such as DGTN, GAP-P, BDNPA/F, that don't swell the NC. Propellants with 50% ball powder and 10% HMX in a plasticized binder have been made that

have go/no-go values in the 70 ± 10 cards range in the NOL Large scale gap test without extensive optimization. Further, the Ball powder system (NC/NG) is low cost, and sensitive to ballistic modifiers such as various bismuth compounds. These compounds can have the same affect as lead catalysts to affect burn rate and lower exponent, but without the environmental impact. The ballistic modifiers must be incorporated into the ball powder to catalyze the combustion. Ballistic control will be a key factor in AP free propellants. Accelerated aging of these propellants have demonstrated lack of plasticizer migration both into the NC from the composite matrix and out of the NC into the synthetic polymer.

As stated in the technical objective above, the performance required is a del-Isp° of at least 248 sec with a del-den-Isp° of 16.2 sec-lb$_m$/in^3. If only 248 sec is obtained, this requires a density of 0.0653 lb/in^3 or 1.808 g/mL. The oxidizers proposed have densities less than AP (1.95 g/mL) and in some cases less than the required 1.808 g/mL. Thus, the high-density oxidizer CL-20 (2.04 g/mL) will also be considered as a supplement to bring up the density of formulations as needed.

Table 4—1. Comparative Data On Various Oxidizers.

Oxidizer	Obal (%, to CO_2)	Obal (%, to CO)	Density (g/mL)
AP	34	-	1.95
ADNA	21	-	1.76
DNNC	13.3	26.7	1.82
HCO	0	17.8	1.875
ADNDNE	0	11.8	1.77
CL-20	-11	11.0	2.04
Ball Powder	-19.3	10.3	1.63

The potential ability of oxidizer combinations in ball powder propellants to replace AP in formulations and meet the performance objectives is shown in **Figure 4—3** and **Figure 4—4** below. The specific formulations are detailed in the figure. As shown, DNNC and HCO oxidizers can meet both the Isp and del-den-Isp requirements in the propellants shown. However, with the ball powder oxidizer one can only meet the Isp objective and not del-den-Isp. This is due to the low density of the ball powder. Using CL-20 or other oxidizers in conjunction with the ball powder can help overcome the deficient density. CL-20 is high density and the other high oxygen oxidizers can allow for more aluminum. This is illustrated in **Figure 4—4**.

A thorough trade study of all the ingredient combinations using design-of-experiment was the first step in the program. This will help identify the best candidate formulations.

Initial formulation of ingredients is necessary to show that they are potential useable. Formulations will be made that meet the performance goals with the new ingredients. Initial formulation was conducted on the 50-600 gram scale. This provided data on processibility, compatibility and sensitivity. Some ballistic testing can also be conducted on mixes of this size. It is expected that there will necessarily be iterations between initial processing and synthesis to arrive at compatible materials with acceptable morphology and sensitivity.
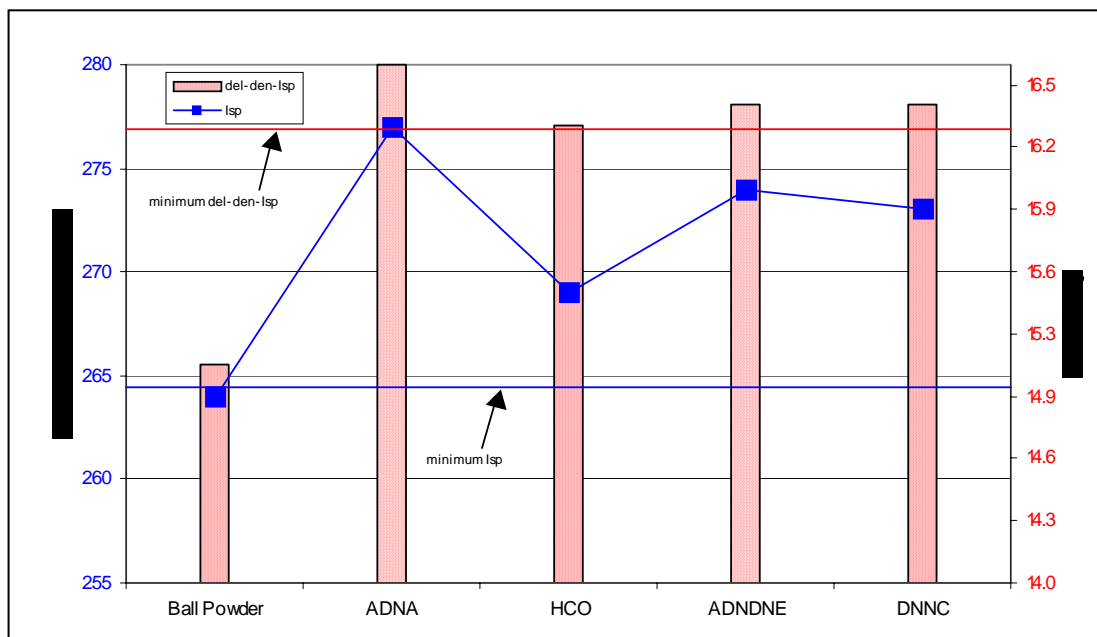
Figure 4—3. Performance data for formulations exploiting alternate oxidizers. Formulations are 60% solids with PGN/DGTN binders Pl/Po = 1.0 with 18 or 20% aluminum depending on OCAL. OCAL's are 1.12-1.18.
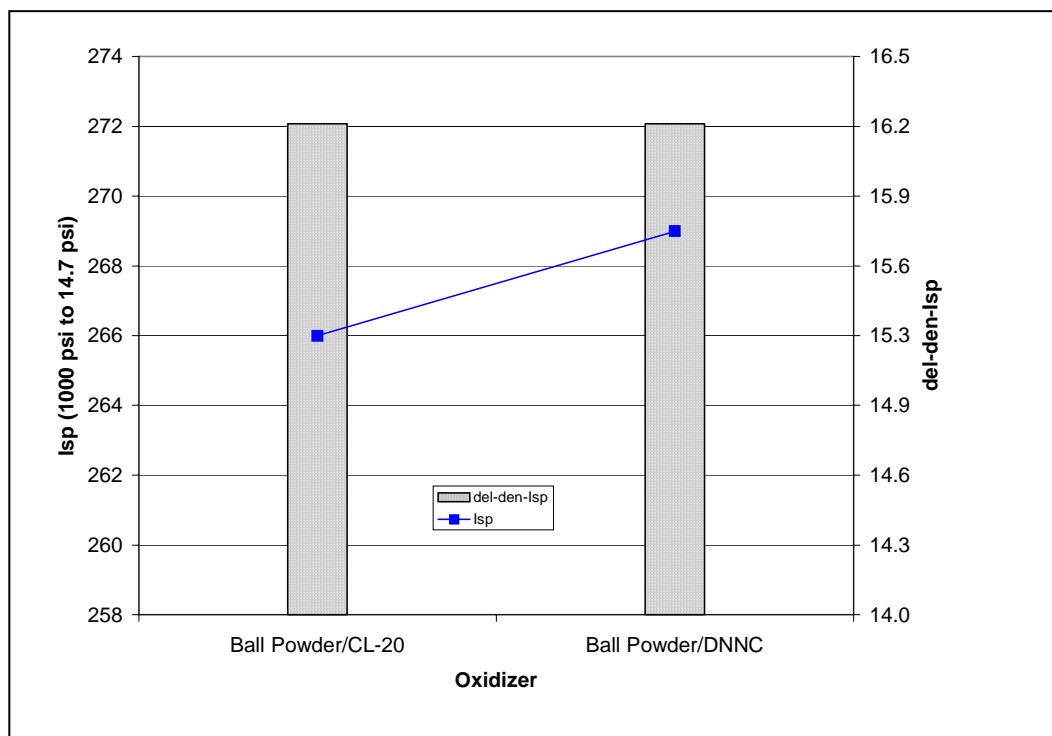

Figure 4—4. Performance data for formulations exploiting alternate oxidizers. CL-20 formulation is 80% solids with 18% Al and 20% CL-20, DNNC formulation is 70% solids with 22% Al and 21% DNNC. Both are with PGN/DGTN binder Pl/Po = 1.0. OCAL's are 1.08-1.09.

5 RESULTS AND ACCOMPLISHMENTS

5.1 NEW OXIDIZER SYNTHESIS

5.1.1 SYNTHESIS OF ADNA

Work on the synthesis of ammonium di-nitramido amine (ADNA) was not been started due to the extra time spent on ADNDNE (see below). However, we developed an additional synthesis route **Figure 5—1** that is based on the reaction of di-*t*-butyl diazene *N*-oxide[4] with nitronium tetrafluoroborate, analogous to the nitration of phenyl *t*-butyl diazene *N*-oxide.[5] Selective reduction of the azoxy functional group by phosphine to the azo compound prepares the desired aza-Michael acceptor for ammonium nitrourethane addition and subsequent removal of the *t*-butyl and ethoxycarbonyl groups by chlorination and ammonolysis procedures. The previously described procedure in our initial proposed work was based on a nitrourethane reaction with an alkyl- or trialkylsilyl-substituted amine with leaving groups such as alkoxy or halogens attached to the amine **Figure 4—2**.
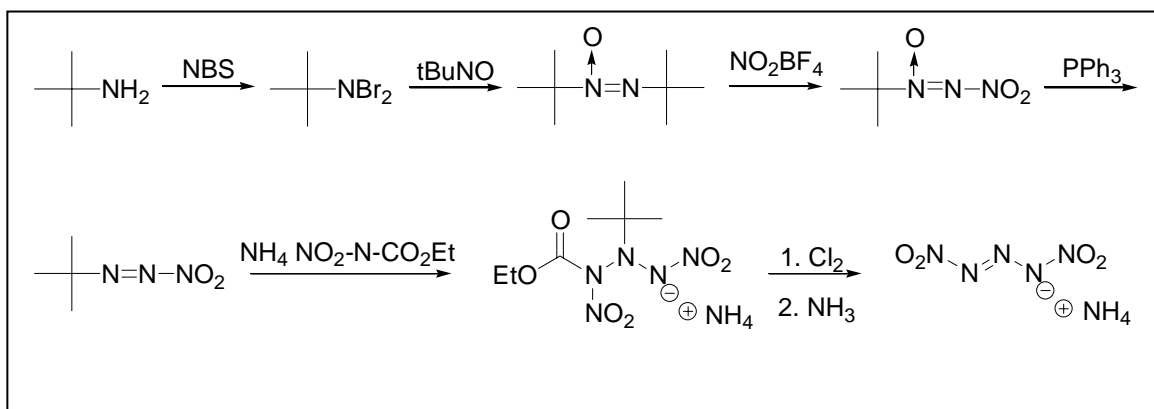
Figure 5—1. New Proposed Synthesis for Ammonium Dinitramido Amine (ADNA).

5.1.2 SYNTHESIS OF ADNDNE

We investigated extensively the synthesis of ADNDNE (ammonium 1,1-dinitramino-2,2-dinitroethylene, **Figure 4—1**). A starting point for this material is FOX-7 (1,1-diamino-2,2-dinitroethylene, **Figure 5—2**).
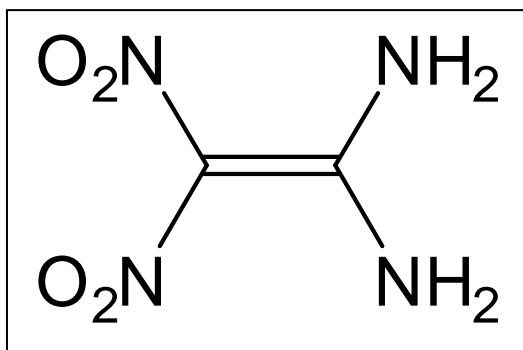
Figure 5—2. Structure of Fox-7 Starting Material.

FOX-7 is a nitro-enamine, possessing a curious duality of reactivity. In reactions with amines, FOX-7 behaves as an electrophile via 1,4 conjugate addition. Although reactions with simple alkyl amines often yield unresolved mixtures of mono- and bis- substituted addition products, reactions with diamines yield cyclic amines in good yield and purity.[6] Conversely, FOX-7 behaves as a nucleophile in amine alkylation and acylation reactions, albeit a poor one; FOX-7 is roughly 25 orders of magnitude less basic than simple alkyl amines (pK_a = 10.6).[6] Indeed, FOX-7 is such a poor nucleophile that *N*-alkylation and *N*-acylation require refluxing conditions.[7]

We observed the formation of the bis-acetamide of FOX-7 (**3**) (**Figure 5—3**) using acetyl chloride and sodium hydride at room temperature **Table 5—1**. In an effort to improve this rather low yield, we attempted to synthesize **3** using acetic anhydride catalyzed by trimethylsilyl triflate (TMSOTf). Although acetic anhydride had failed to even mono-acetylate FOX-7 under various reaction conditions before, we now observe FOX-7 conversion. Unfortunately, addition of methanol to this anhydrous reaction mixture regenerates the starting material, FOX-7.
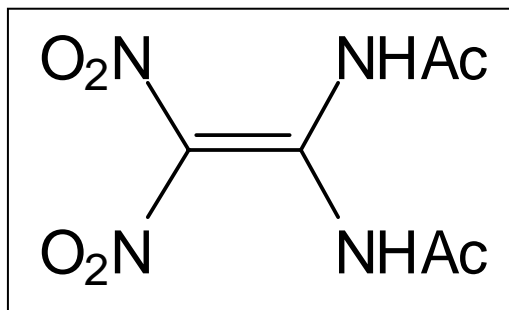
Figure 5—3. bis-acetamide of FOX-7.

Table 5—1. Mono- and Bis- Acetamide of FOX-7.

|	Reaction Conditions				**Mono**	**Bis**
a)	Ac$_2$O	-	AcOH	25 ℃	NR	NR
b)	Ac$_2$O	DMAP / Et$_3$N	CH$_3$CN	25 ℃	0	0
c)	Ac$_2$O	NaH	DMF	25 ℃	0	0
d)	Ac$_2$O	TMSOTf	CH$_3$CN	4 ℃	0	0
e)	AcCl	NaH	DMF	25 ℃	0	0
f)	AcCl	NaH	CH$_3$CN	25 ℃	~16	~8
g)	AcCl	NaHMDS	THF-CH$_3$CN	25 ℃	~10	~5

Similar transacylation reactions have also been reported for the hydrolysis and methanolysis of the FOX-7 oxamide (**4**) **Figure 5—4,** yielding FOX-7.[8] Indeed, the original preparation of FOX-7 involved the aqueous ammonolysis of **4**. Since acylated derivatives of FOX-7 appear to be labile to hydrolysis and/or alcoholysis, we abandoned this indirect approach of amine acylation in our efforts to synthesize **ADNDNE**.
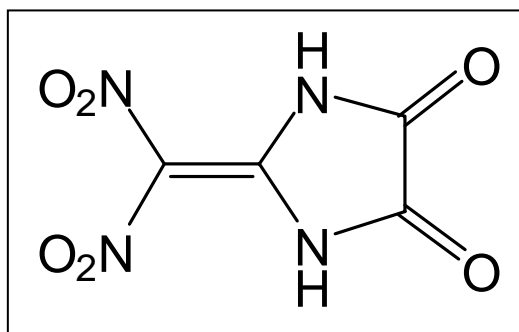
Figure 5—4. The FOX-7 oxamide (4).

Although alkylation and silylation still remain viable amine derivatization strategies, we decided to focus on direct *N*-nitration using non-acidic conditions to synthesize the FOX-7 bis-nitramine **Figure 5—5**. Acetyl nitrate was not strong enough to nitrate FOX-7. However, we believe we are able to N-nitrate FOX-7 using trifluoroacetyl-nitrate, which was prepared immediately prior to FOX-7 addition. This is necessary since FOX-7 decomposes in neat trifluoroacetic anhydride. Although ammonium nitrate and trifluoroacetic anhydride appears to give better yields and purity than does 98% nitric acid and trifluoroacetic anhydride, the yields listed are approximate and not actual yields. Isolation has been difficult, perhaps due to decomposition and/or hydrolysis of the expected product. We envisioned that cupric nitrate and trifluoroacetic anhydride might overcome the decomposition problem by forming the cupric di-nitramine salt, however our brief attempts were unsuccessful. The difficulty in isolation of a pure product and

the possibility of instability of the acidic N-H product were considered and the direct nitration process was abandoned.
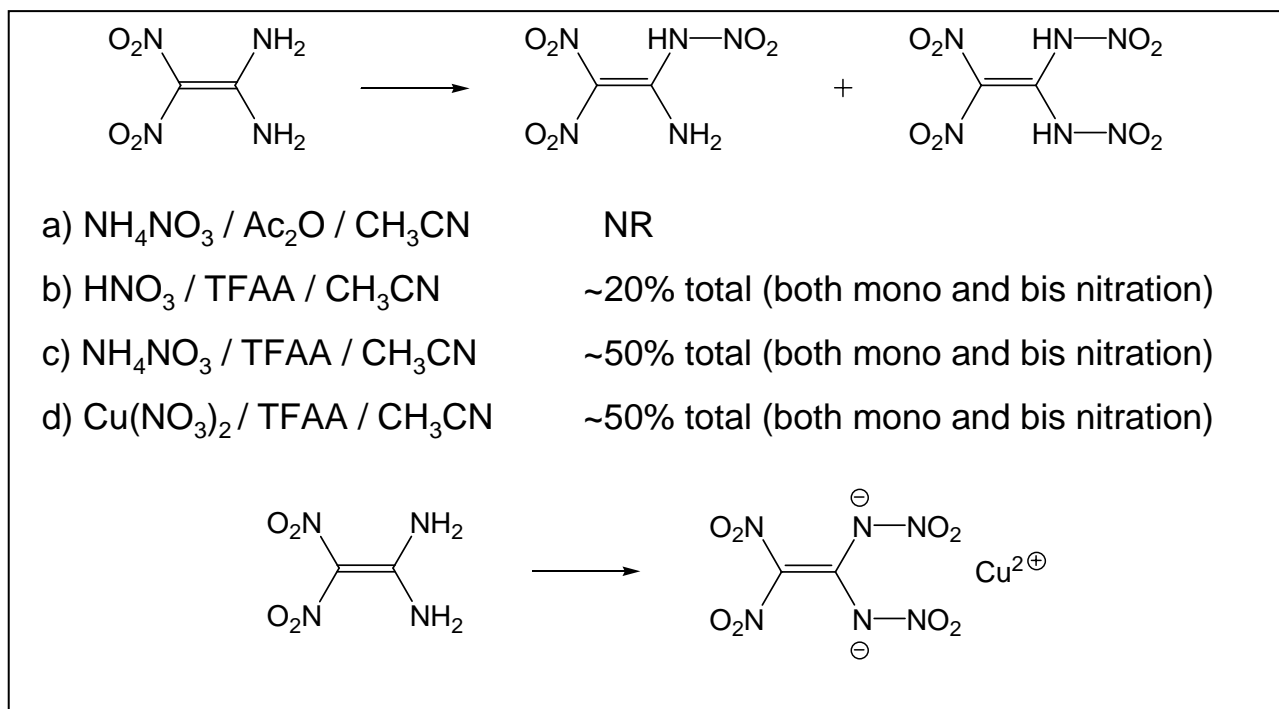
Figure 5—5. Direct Nitration Efforts

We also tried to synthesize the bis-trifluoroacetamide of FOX-7 **Figure 5—6**, but we only observed decomposition to volatile species, presumably lower molecular weight species. Perhaps the carbon-carbon bond of FOX-7 is cleaved to yield an unidentified dinitromethane species in the presence of trifluoroacetic anhydride. Interestingly, this decomposition does not occur in trifluoroacetic acid itself.
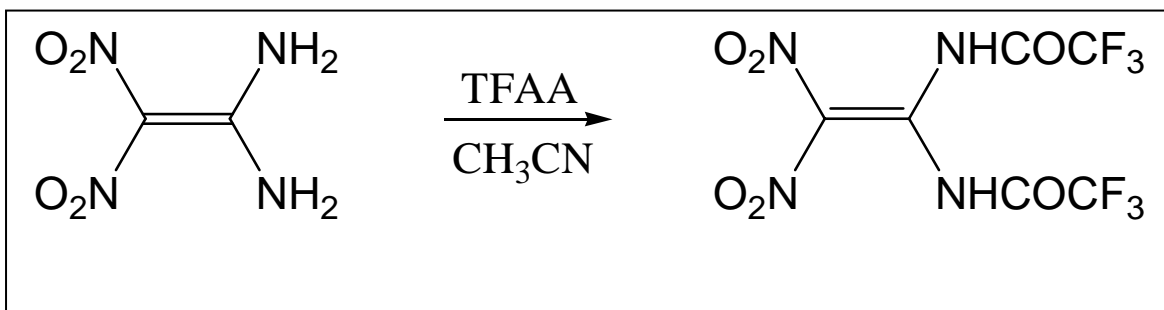
Figure 5—6. Trifluoroacetamide Synthesis.

Although FOX-7 is a very poor nucleophile, its anion is expected to be more reactive in electrophilic reactions, such as nitration, alkylation, acylation, and silylation. We have synthesized the previously unprepared potassium salt of FOX-7 in quantitative yields, and we will begin nitration of this salt immediately. A caveat, however, is that the control of regioselectivity (*N*- vs *C*- or *O*-nitration) remains a significant challenge.

Instead of an electrophilic approach, an alternative retrosynthetic analysis of **1** involves nucleophilic reactions with diiodo-dinitroethylene **Figure 5—7**. Baum et al. has shown that diiodo-dinitroethylene undergoes nucleophilic attack with various amines, although not with ammonia, forming FOX-7 derivatives.[9] We have reproduced the difficult synthesis of diiodo-dinitroethylene**,** and we plan to form **ADNDNE**, using *N*-nitrourethane as a nucleophile, wherein the first-formed bis(N-nitrourethane) substitution product is subjected to an ammonolysis reaction.
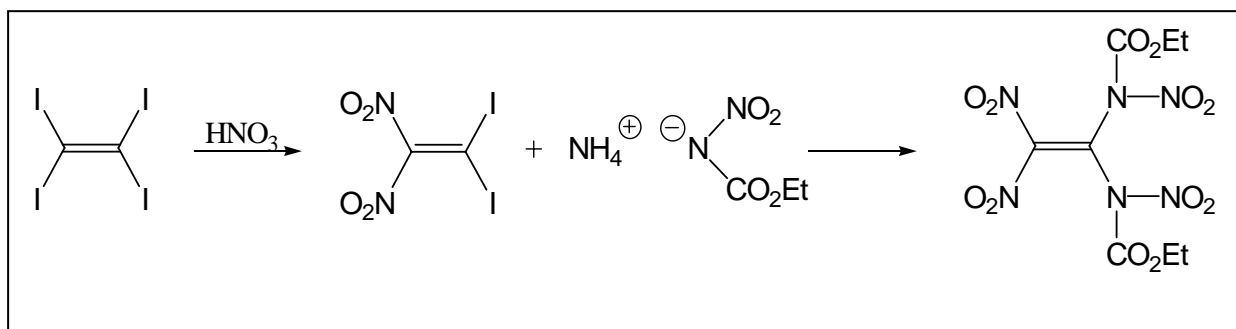
Figure 5—7. Nucleophilic reactions with diiodo-dinitroethylene.

Our immediate focus is to derivatize the potassium salt of FOX-7 **Figure 5—8**. Acetic anhydride is not strong enough to acylate the potassium salt. We recently found that Boc anhydride does react with the potassium salt, and we were isolating the products when the program was terminated -- many FOX-7 derivatives appear to be water sensitive.
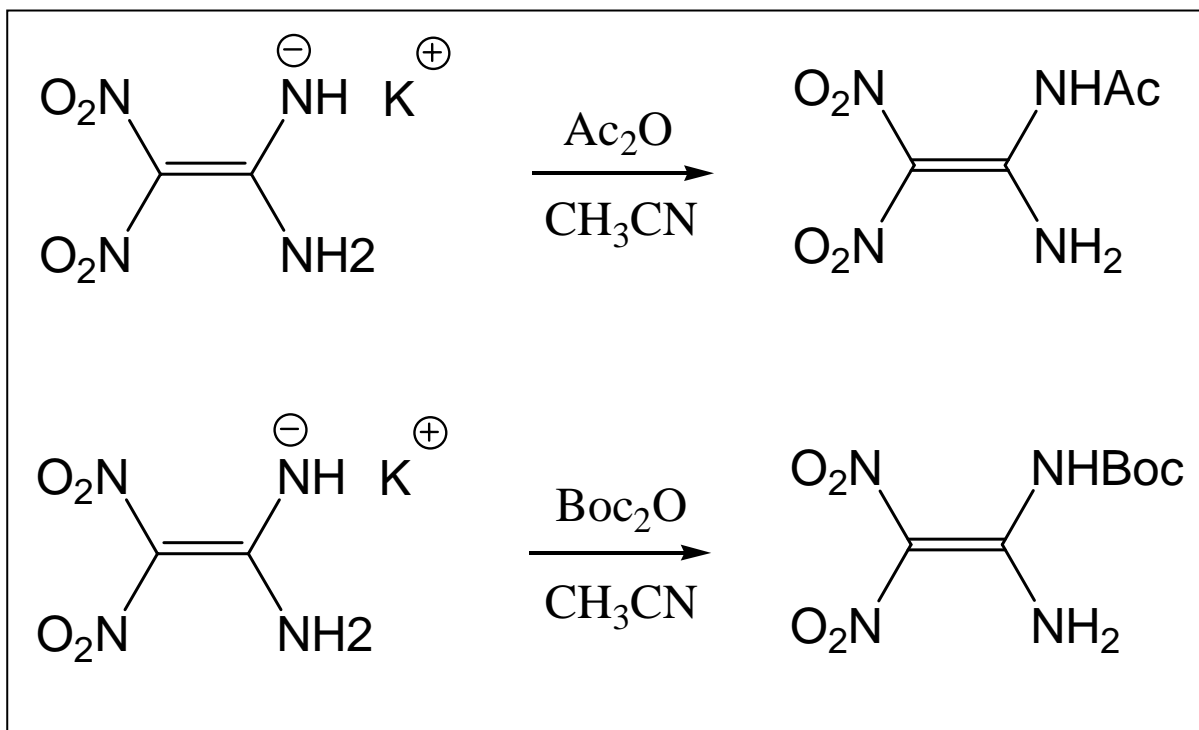
Figure 5—8. Acylations of FOX-7 Potassium Salt.

We decided to N-nitrate a FOX-7 salt instead. The same group from FOI (the Swedish Defence Research Agency), who had originally published the FOX-7 synthesis in 1998, had also reported the isolation of the guanidinium salt of FOX-7. We were able to make a guanidinium salt of FOX-7 using the free base of guanidine, generated from the guanidinium carbonate by either heating it in solution to drive off the carbonic acid, or by neutralizing it with aqueous calcium hydroxide, and then filtering off the insoluble calcium carbonate.

Unfortunately, the guanidinium salt of FOX-7 failed to N-nitrate, using either n-propyl nitrate by itself or n-propyl nitrate with BF3, which generates an in situ nitronium source as NO_2BF_4 **Figure 5—9**. Perhaps the majority of the electron density in the FOX-7 anion resides on the carbon.

a) nPrONO$_2$ / CH$_3$CN   NR
b) nPrONO$_2$ / BF$_3$-Et$_2$O / CH$_3$CN   0%
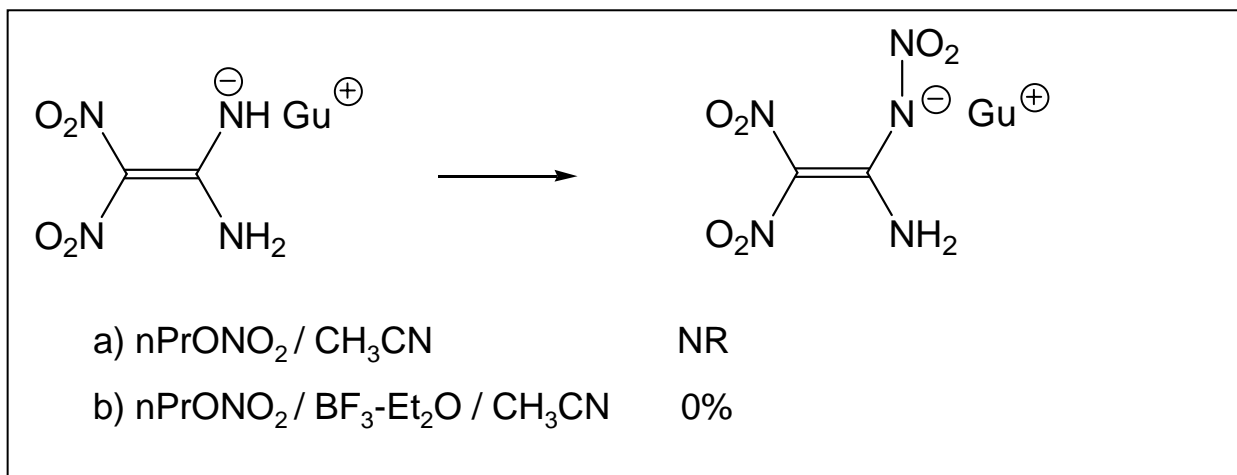
Figure 5—9. Nitration of FOX-7 Salts.

5.1.3 SYNTHESIS OF HCO.

The synthetic route to HCO has not lent itself as readily to scale-up **Figure 5—10**. The process, which is six steps from A-diol, has presented with a number of undesirable attributes. Two of the key intermediates, potassium dinitroethanol and dipotassium bis(dinitroethyl)amine, are highly unstable and should not be stored (especially dry) for any appreciable length of time. In addition, the nitration of dipotassium bis(dinitroethyl)amine will require considerable route development to improve safety and yields. Finally, the nitration of 1,3,3,7,7-pentanitro-1,5-diazocine will need to be improved to give cleaner HCO, as purification of the current material is proving quite tedious. **Figure 5—10** shows the current synthetic route to HCO. All of the reactions up to the synthesis of 1,3,3,7,7-pentanitro-1,5-diazocine have been performed at the 10 gram scale or higher. Safety data for three intermediates are given in **Table 5—2**.
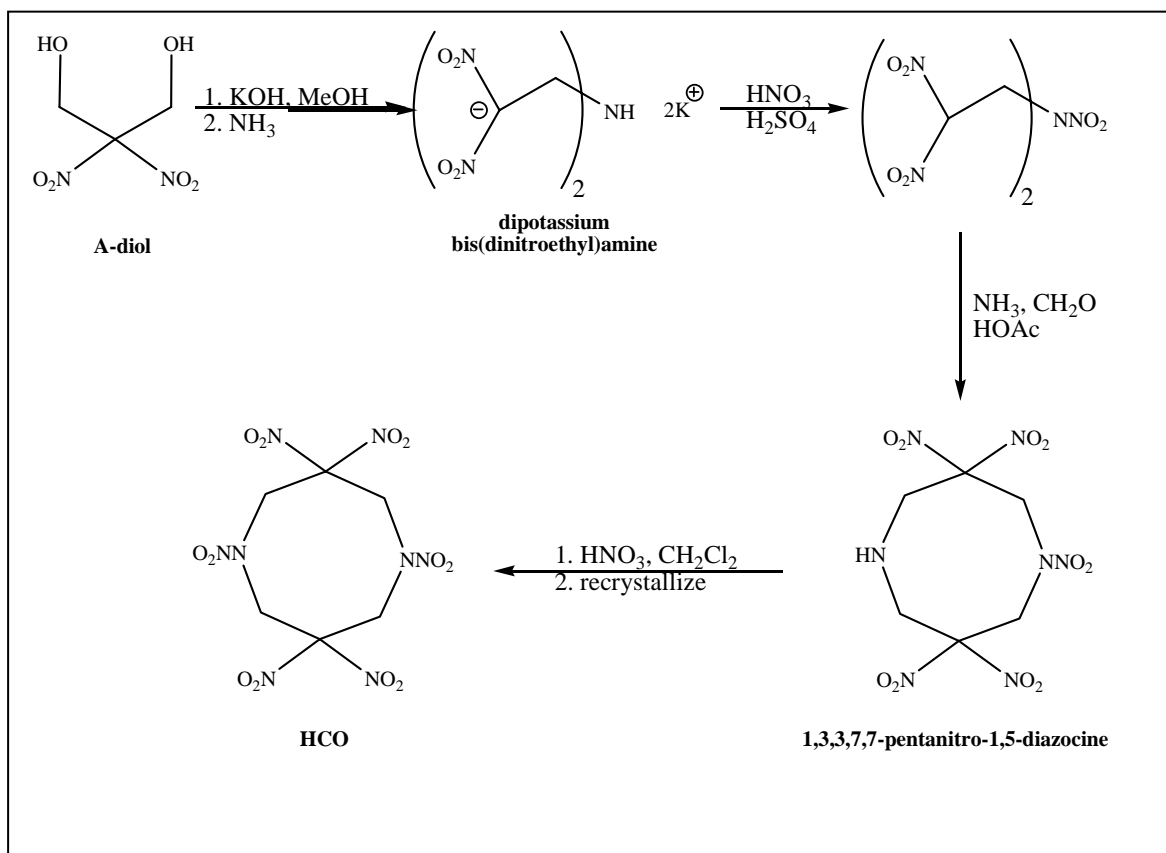
Figure 5—10. HCO Synthesis

Table 5—2. Safety data for HCO intermediates Figure 5—10.

	2K$^+$ bis(dinitroethyl)amine	bis (dinitroethyl)nitramine	pentanitro-1,5-diazocine
ABL impact (cm)	1.8	80	33
ABL friction (lbs)	800 @ 8 ft/s	800 @ 8 ft/s	800 @ 8 ft/s
TC ESD, unconfined (J)	1.5, no bulk ignition	>8	0.13, mass ignition
SBAT onset (°F)	204, exploded	111, burned	180, burned
TC impact (in)	43.4	>46	>46

5.1.4   SYNTHESIS OF DNNC

The synthesis of DNNC proceeds quite smoothly in a 68% overall yield from 2,2-dinitro-1,3-propanediol (A-diol). The three-step process, outlined in **Figure 5—11** below, has yielded approximately 35 grams of pure DNNC for testing and evaluation. The material has a melting point of 153-154°C, and an HPLC purity of 99.3%. The results of small-scale safety testing and additional thermal analysis data are reported in **Table 5—3**.
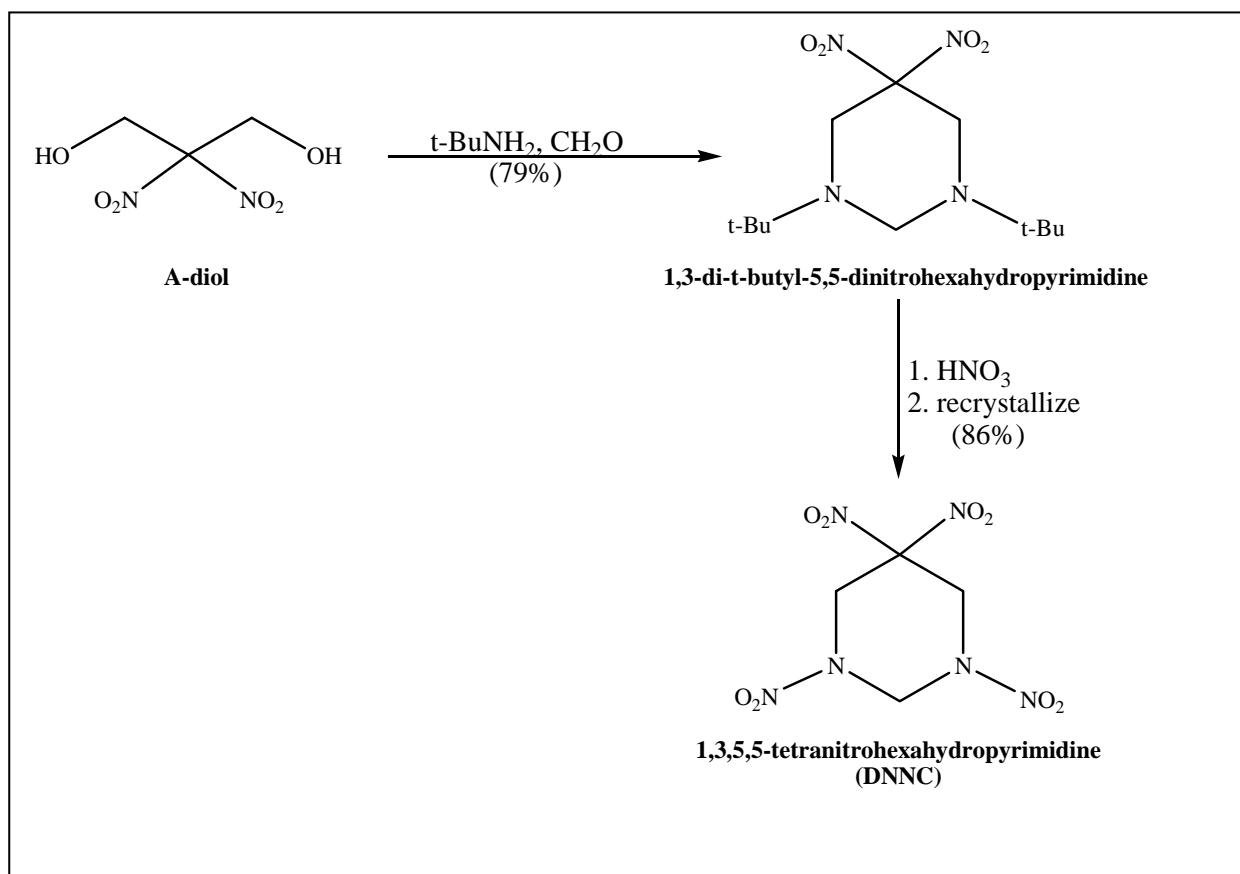
Figure 5—11. DNNC Synthesis.

Table 5—3. Safety and thermal data for DNNC and its precursor.

	1,3-di-t-Bu-5,5-dinitrohexahydropyrimidine	DNNC
ABL impact (cm)	80	3.5
ABL friction (lbs)	800 @ 8 ft/s	660 @ 8 ft/s
TC ESD, unconfined (J)	< 0.05	1.90, no bulk ignition
SBAT onset (°F)	153, burned	317
TC impact (in)	> 46	25.5
DSC onset, peak (°C)	--	219, 227

5.1.5 CONCLUSIONS

Extensive attempts to synthesize ADNDNE were unsuccessful. Synthesis routes starting with the commercially available FOX-7 (**Figure 5—3**) were extensively examined. The first idea examined was to derivatize the amine functionality of FOX-7 and then nitrate the derivative yielding the desired product. Reaction conditions were found for the acylation of FOX-7 with acetyl chloride and acetic anhydride. However, the resulting derivatives are labile to hydrolysis and alcoholysis. Thus we concluded that acyl derivatives are not good candidates for nitration to the desired product.

Direct nitration of the FOX-7 was accomplished using ammonium nitrate and trifluoroacetic anhydride. However, the product was unstable under the extreme nitration conditions required, which prevented isolation of the desired product prior to significant decomposition. Thus, we concluded that this method is not a good candidate for synthesis of the desired product.

Direct nitration of the potassium salt of FOX-7 may work to prepare the desired product, but this method was not fully examined before the program was terminated. However, Nitration of the known guanidinium salt of FOX-7 was not successful and we determined it is not a good candidate for making the desired product.

Making non-acyl derivatives of the FOX-7 via the potassium salt (e.g. Boc derivatives) and derivatization of the diiodo-dinitroethylene followed by nitration are promising methods that were not fully developed before the program was terminated. Even though ADNDNE has proven elusive, we believe it is likely that ADNDNE could be produced by one of these unexplored methods. However, no ADNDNE was produced on the program.

The extra time spent on ADNDNE resulted in essentially no effort being spent on ADNA. We believe it could be synthesized by the method discussed but no work was accomplished to prove this idea.

The intermediates for HCO were too hazardous to make scale up feasible. A small amount of HCO was made for characterization, but new synthetic methods will be needed for scale up. Thus, we concluded that it is not practical to pursue HCO on this program. The compound was dropped.

The DNNC material was produced relatively easily at the 25 gram scale. Scale up was in progress when the program was terminated. We concluded it is a good candidate supplemental oxidizer for the program.

5.2   ENVIRONMENTAL SCREENING

5.2.1   FATE AND TRANSPORT SCREENING

5.2.1.1   Introduction

A task was completed to estimate, based on quantitative structure activity relationships (QSAR), the fate-and-transport and toxicological properties of new oxidizers proposed to replace perchlorate in rocket propellant formulations. The fate-and-transport and toxicological properties of the new oxidizers shown in **Figure 4—1** were estimated and compared to perchlorate to determine if they are more or less environmentally benign relative to perchlorate. This work is reported in the technical report entitled "Final Environmental Screening Assessment of Perchlorate Replacements Report" prepared by AMEC Earth & Environmental; Boston, Massachusetts. The full AMEC report is included as an appendix.

5.2.1.2   Discussion

The conclusions made are based on four important predicted parameters:

1. Water solubility
2. Octanol/Water partition coefficient (log K_{ow})
3. Organic/Carbon partition coefficient (K_{oc})
4. Photolysis half-life

Lower water solubility is better for transport as the compound will be less mobile in ground or surface water if it is less soluble. Higher log K_{ow} is better as long as the value stays below 1. Higher K_{ow} means more affinity for lipids making the compound less mobile in water. However, compounds with values greater than 1 will biomagnify in the food chain having adverse affects. None of the compounds including AP are a concern based on K_{ow}. Higher K_{oc} is better as the compound will tend to adsorb onto soil and clay more. This will reduce mobility in ground water. A shorter photolysis half-life is better as the compound will degrade faster.

Table 5—4 below details the four parameter values for each compound of interest.

Table 5—4. Environmental fate and transport parameter values for each compound.

Compound	Predicted water solubility (mg/L)	Predicted log K_{ow}	Predicted K_{oc}	Predicted photolysis half-life
AP	1,000,000	-5.85	96.6	NA[1]
ADNA	115,600	-0.14	3.4	Minutes[2]
ADNDNA	232,800	-1.54	928	Minutes[2]
DNNC	50,100	-1.14	1678	NA[1]
HCO	153,00	-2.8	137,000	NA[1]

[1]no photolysis expected

[2]based on literature data on the analogous compound ADN (Mill and Spanggord, 1997)

Based on discussions above, each compound can be ranked for fate and transport based on it value for each parameter. This is shown in **Table 5—5** below.

Table 5—5. Compounds of interest ranked according to environmental fate and transport.

Compound	Predicted water solubility rank	Predicted log K_{ow} rank	Predicted K_{oc} rank	Predicted photolysis half-life rank
AP	5	5	4	3
ADNA	2	1	5	1
ADNDNA	4	3	3	1
DNNC	1	2	2	3
HCO	3	4	1	3

5.2.1.3   Conclusions On Fate and Transport

1. The four compounds in **Figure 4—1** are predicted to have a low lipophilic nature as shown by low predicted log K_{ow} coefficients. This favors migration to surface water or ground water but also indicates these compounds would not bioconcentrate into aquatic organisms or biomagnify within the food chain. Direct toxicity to aquatic organisms is also predicted to be very low.
2. Compared to AP, the compounds are anticipated to behave similarly from an environmental fate and transport perspective. However, each of the compounds, are

either much less soluble in water than AP or are expected to adsorb onto clay and soil better or will readily photodegrade. It is reasonable that each of these four compounds would be an improvement over AP for fate and transport.

3. The compound are ranked currently DNNC, ADNA, HCO, ADNDNE according to the method described.

4. The method employed exhibits a lack of accuracy predicting some critical parameters (melting point, water solubility, K_{oc}) in some cases. The lack of empirical data limits how well the materials can be compared to AP at this point. It is recommended that further literature searches be done to generate more empirical data and/or this data be collected on the compounds themselves once samples are available from the synthesis labs.

5.2.2 PREDICTONS MAMMALIAN TOXICITY, METABOLISM AND/OR ENVIRONMENTAL DEGRADATION

5.2.2.1 Introduction

Following the evaluation of fate-and-transport of the above compounds using EPI Suite, the next logical step was to evaluate QSAR models that may be able to predict mammalian toxicity, metabolism and/or environmental degradation. A careful web based search identified the Bio-Rad "ADME/Tox" Know-It-All model, from the perspective of cost/benefit, as the most effective QSAR routine on the market. Once this model could be learned and run effectively, it would be able to achieve the goal of estimating toxicity, degradation and metabolism of the above perchlorate replacement compounds. This work is reported in the technical report entitled "Toxicological Screening of Perchlorate Replacements Using the Commercial Bio-Rad "ADME/Tox" Model" prepared by AMEC Earth & Environmental; Boston, Massachusetts. The full AMEC report is included as an appendix.

5.2.2.2 Results

Table 5—6 presents the Predicted Toxicity Report Summary for all of the compounds simulated on the ADME/Tox software. The only "Alerts" generated were for "Oncogenicity" (potential to induce cancer) and "Mutagenicity" (potential to cause a mutation) for the both the DNNC/RDX and HCO/HMX pairs. This result indicates that the choice of the surrogate analog compounds for both DNNC and HCO were most likely correct as the model responded to them in the exact same way. The simulation of the remaining compounds resulted in an output of "zero". Bioaccumulation scores ranged from 66 (FOX-7) to 100 HCO/HMX, meaning that most of the compounds tested by the computer program had a moderate to very strong propensity to bioaccumulate in an organism.

Table 5—6. Predicted Toxicity Report Summary

Compound:	RDX	DNNC	HMX	HCO	ADN	ADNA	FOX-7	ADNDNE
Oncogenicity	82	82	82	82	0	0	0	0
Mutagenicity	75	75	75	75	0	0	0	0
Teratogenicity	0	0	0	0	0	0	0	0
Immunotoxicity	0	0	0	0	0	0	0	0
Neurotoxicity	0	0	0	0	0	0	0	0
Irritation	0	0	0	0	0	0	0	0
Sensitivity	0	0	0	0	0	0	0	0
Bioavailability	0	0	0	0	0	0	0	0
Bioaccumulation	91	91	100	100	91	91	66	91

Table 5—7 presents the Predicted Metabolism Report Summary for all of the compounds simulated with the metabolism subroutine. Because metabolic reactions can often lead to the formation of multiple metabolites (generated from a single parent compound), some of the simulation runs were run with more than one "Metabolic Steps". Therefore, some of the output may seem redundant because the computer program was set to process more than two steps. For example, if compound was hydrolyzed, it is possible that the reactive product may then be conjugated to an endogenous compound, such as a glucuronide.

Table 5—7. Predicted Metabolism Report Summary.

Compound	ADNA	ADN	ADNDNE	FOX7	DNNC	RDX	HCO	HMX
Metabolism								
Plant	NR	NR	NR	NR	NR	NR	NR	NR
Photodegradation	NR	NR	NR	NR	P	P	P	P
First Pass	NR	NR	NR	P	NR	NR	NR	NR
Animal	NR	NR	P	P	NR	NR	NR	NR
Predicted	P							
No Results	NR							
Specific Results are attached								

5.2.2.3   Conclusions - Toxicity

None of the parent compounds that were processed for toxic endpoints using the ADME/Tox model showed any "response" for teratogenicity, irritation, sensitivity, immunotoxicity, neurotoxicity or bioavailability. Although much of this "negative data" appears suspicious, a call to the Bio-Rad technical representative assured us that a "zero result" does not mean that the

chemical was not processed by the respective subroutine. To the contrary, it means that the chemical has a very low potential to cause toxicity for that particular toxic effect category. From the standpoint of perchlorate replacements, this is good news in that the screening process for the replacement compound showed no "positive" result.

One concern may be the fact that DNNC, RDX, HCO and HMX showed some potential for oncogenicity and mutagenicity. That result, however, appears to be based on the presence of a nitroso- group within the ring structure. Since the carcinogenic activity of nitrosamine compounds is principally a function of primary amine groups, it is unlikely that the secondary or tertiary nitroso- groups within these energetic munitions compounds would be able to show carcinogenic activity. It is already known that RDX will not cause mutations in laboratory tests, but it does have the potential to cause cancer in laboratory animals (although the evidence is not strong). There is also no evidence that exists to show RDX causes cancer in humans.

DNNC, RDX, HCO and HMX all showed the potential, according to the ADME/Tox output, to undergo photodegradation. It is interesting, from this viewpoint, that ADNA, ADN and ADNDE did not respond to the photodegradation model because EPI Suite showed that most of these munitions compounds had the potential to photodegrade.

This research has shown that the ADME/Tox software has many different powerful evaluative tools available to assess the physical, chemical and biological parameters for a host of different organic compounds. Unfortunately, the fact that 56 out of a total of 64 toxicity endpoints (8 compounds x 8 endpoints) ended up with a result of "zero" leaves the user with a strong impression that the model is not "sensitive" when it comes to discerning adverse effects. This may simply be a result of the content of the "training set" used to construct the QSAR subroutines within the model. For example, if there are very few compounds that contain two or more nitrogens, the "confidence" of the model may not be high and therefore the decision process may instruct the model to use a "zero" for the result (even though the compound being modeled may fall within the "chemical space" of the QSAR training set).

5.3 PROPELLANT FORMULATION

5.3.1 PROPELLANT PERFORMANCE TRADE STUDY

A propellant performance trade study was completed for the 4 new oxidizers being synthesized on the program plus CL-20 **Figure 5—12**. These oxidizers are to replace AP when used in combination with Ball Powder.

The methodology used is to perform a 5 component Design of Experiment. The five formulation components are: Prepolymer, Plasticizer, Ball Powder, Aluminum, and supplemental oxidizer. Using this method the optimum combination of the five components can be determined based on the responses of Isp, den, Den-Isp, and Volume% liquid, and O/F ratio. Of course multiple solutions are produced and the best is selected based on minimizing ingredients which are known to increase shock sensitivity.

The most promising formulations are shown below in Tables **Table 5—8**, **Table 5—9**, , **Table 5—10**, , **Table 5—11**, **Table 5—12**.

Table 5—8. Formulation with CL-20 Supplemental Oxidizer.

Ingredient	Weight%
PGN	10.30
DGTN	19.55
Ball Powder	35.58
Al	21.90
CL-20	12.67
Performance	
Isp (lb$_f$-sec/lb$_m$)	266.6
Density (lb/in^3)	0.06457
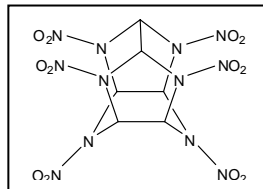
Figure 5—12. Structure of CL-20.

Table 5—9. Formulation with DNNC Supplemental Oxidizer.

Ingredient	Weight%
PGN	10.00
DGTN	19.72
Ball Powder	33.64
Al	23.82
DNNC	12.82
Performance	
Isp (lb$_f$-sec/lb$_m$)	266.9
Density (lb/in^3)	0.06426

Table 5—10. Formulation with HCO Supplemental Oxidizer.

Ingredient	Weight%
PGN	10.95
DGTN	12.54
Ball Powder	36.88
Al	21.02
HCO	18.61
Performance	
Isp (lb$_f$-sec/lb$_m$)	266.9
Density (lb/in^3)	0.06444

Table 5—11. Formulation with ADNDNE Supplemental Oxidizer.

Ingredient	Weight%
PGN	10.49
DGTN	19.54
Ball Powder	24.51
Al	19.80
ADNDNE	25.66
Performance	
Isp (lb$_f$-sec/lb$_m$)	270.0
Density (lb/in^3)	0.06359

Table 5—12. Formulation with ADNA Supplemental Oxidizer.

Ingredient	Weight%
PGN	16.43
DGTN	16.09
Ball Powder	21.31
Al	22.87
ADNA	23.30
Performance	
Isp (lb_f-sec/lb_m)	269.5
Density (lb/in^3)	0.06387

5.3.2 INITIAL FORMULATION CHARACTERIZATION

A formulation based on the one shown in Figure 1 was made and characterized in the NOL Large Scale Gap Test. The formulation was modified slightly by adjusting the curative to polymer ratio and a nitrate ester stabilizer was added. The final formulation characterized is shown in **Table 5—13** below.

The result of the NOL LSGT at 70 cards is shown below in **Figure 5—13**. This result is a GO. A GO value was also observed at 80, 90, 100, and 120 cards.

Table 5—13. Formulation Characterized in the NOL LSGT.

PGN	8.335
DGTN	19.56
Ball Powder	35.58
Al	21.90
CL-20	12.67
N-3200	1.445
MNA	0.500
DBTDL	0.010
Isp (lb_f/sec-lb_m)	266.5
Density (lb/in^3)	0.06418

Figure 5—13. Result of NOL LSGT at 70 cards. Result is "GO".

5.3.3 PROPELLANT CONCLUSIONS

The propellant trade study revealed propellant formulations using ball powder and a supplemental oxidizer replacing AP that can meet the performance goals of the program. Initial formulation characterization on the Ball powder CL-20 example revealed shock sensitivity much greater than anticipated. The formulation gave a GO result in the Large Scale Gap Test at 120 cards. A Hazard Class 1.3 propellant would be expected to be a NO GO at 70 cards in the test. State of the art Class 1.1 formulations have NO GO values about 130 cards in this test, but they have more performance. Thus this technology to replace AP results in propellant formulations that have Class 1.3 performance with Class 1.1 hazard properties. Since Class 1.3 is a requirement, it does not appear practical to use this technology to replace AP.

6   PROGRAM CONCLUSIONS

Part of the program involved the synthesis of new oxidizers to use as supplements to the ball powder. The first compound attempted was ADNDNE. All attempts to synthesize ADNDNE were unsuccessful. The approach was to start with commercially available FOX-7 (**Figure 5—3**). Reaction conditions were found for the acylation of FOX-7 with acetyl chloride and acetic anhydride. However, the resulting derivatives are labile to hydrolysis and alcoholysis. Thus we concluded that acyl derivatives are not good candidates for nitration to ADNDNE. Direct nitration was accomplished using ammonium nitrate and trifluoroacetic anhydride. However, the ADNDNE was unstable under these extreme nitration conditions, which prevented isolation. Thus, we concluded that this method is not a good candidate for synthesis of ADNDNE. Also, Nitration of the known guanidinium salt of FOX-7 was not successful and we determined it is

not a good candidate for making the desired product. However, three methods still offer promise for the synthesis of ADNDNE and were not fully examined before termination of the program. These are 1) direct nitration of the potassium salt of FOX-7 and 2) making non-acyl derivatives from the FOX-7 via the potassium salt (e.g. Boc derivatives) followed by nitration and 3) derivatization via the diiodo-dinitroethylene followed by nitration.

A small amount of HCO was made for characterization but the intermediates are too hazardous to make scale up feasible. New synthetic methods will need to be developed prior to scale up of this material. Thus, we concluded that it is not practical to pursue HCO on this program. The compound was dropped. The DNNC material was produced relatively easily at the 25 gram scale. Scale up was in progress when the program was terminated. We concluded it is a good candidate supplemental oxidizer for the program.

The four compounds in **Figure 4—1** were examined for their fate and transport properties. They are predicted to have a low lipophilic nature as shown by low predicted log K_{ow} coefficients. This favors migration to surface water or ground water but also indicates these compounds would not bioconcentrate into aquatic organisms or biomagnify within the food chain. Direct toxicity to aquatic organisms is also predicted to be very low. Compared to AP, the compounds are anticipated to behave similarly from an environmental fate and transport perspective. However, each of the compounds, are either much less soluble in water than AP and/or are expected to adsorb onto clay and soil better or will readily photodegrade. It is reasonable that each of these four compounds would be an improvement over AP for fate and transport.

None of the parent compounds that were processed for toxic endpoints using the ADME/Tox model showed any "response" for teratogenicity, irritation, sensitivity, immunotoxicity, neurotoxicity or bioavailability. This means that the chemical has a very low potential to cause toxicity for that particular toxic effect category. From the standpoint of perchlorate replacements, this is good news in that the screening process for the replacement compound showed no "positive" result.

One concern may be the fact that DNNC, RDX, HCO and HMX showed some potential for oncogenicity and mutagenicity. That result, however, appears to be based on the presence of a nitroso- group within the ring structure. Since the carcinogenic activity of nitrosamine compounds is principally a function of primary amine groups, it is unlikely that the secondary or tertiary nitroso- groups within these energetic munitions compounds would be able to show carcinogenic activity. It is already known that RDX will not cause mutations in laboratory tests, but it does have the potential to cause cancer in laboratory animals (although the evidence is not strong). There is also no evidence that exists to show RDX causes cancer in humans.

DNNC, RDX, HCO and HMX all showed the potential, according to the ADME/Tox output, to undergo photodegradation. It is interesting, from this viewpoint, that ADNA, ADN and ADNDE did not respond to the photodegradation model because EPI Suite showed that most of these munitions compounds had the potential to photodegrade.

The propellant trade study revealed propellant formulations using ball powder and a supplemental oxidizer replacing AP that can meet the performance goals of the program. Initial formulation characterization on the Ball powder CL-20 example revealed shock sensitivity much greater than anticipated. Thus this technology examined to replace AP results in propellant formulations that have the desired performance but with the hazard properties of much higher

performing propellants. Since Class 1.3 is a requirement, it does not appear practical to use this technology to replace AP.

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8 APPENDICES

8.1 FATE AND TRANSPORT FINAL REPORT FROM AMEC (CLICK BELOW)

amec

Final Environmental Screening Assessment of Perchlorate Replacements Report

Conducted in Support of the
Strategic Environmental Research & Development Program
"Synthesis, Evaluation, and Formulation Studies on New Oxidizers
as Alternatives to Ammonium Perchlorate in DoD Missile Propulsion Applications."

Submitted to:

Naval Surface Warfare Center
Indian Head, MD

Submitted by:

AMEC Earth & Environmental
Boston, Massachusetts

24 November 2004

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Final Environmental Screening Assessment of Perchlorate Replacements Report

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EXECUTIVE SUMMARY

AMEC Earth & Environmental (AMEC) conducted a screening level assessment of the fate, transport, and toxicity of four potential replacements for perchlorate. The data derived from this project will be helpful in evaluating and minimizing potential environmental liability associated with the use of energetic compounds as propellants. This report details the methods used and the findings of our assessment.

The compounds evaluated in this screening level assessment include the inorganic oxidizer ammonium di (nitramido) amine (ADNA); the cyclic nitramine/gem-dinitro compound 1,3,5,5-tetranitrohexahydropyrimidine (DNNC); 1,3,3,5,7,7-hexanitro-1,5-diazacyclooctane (HCO); and diammonium di(nitramido) dinitroethylene (ADNDNE). In addition to these, AMEC evaluated the following analogue compounds that are currently in use: ammonium dinitramide (ADN) as an analogue for ADNA; hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX) as an analogue for DNNC; octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX) as an analogue for HCO; and 1,1-diamino-2,2-dinitroethene (FOX-7) as an analogue for ADNDNE. Finally, ammonium perchlorate was evaluated as the basis for comparison.

Empirically derived literature values and Quantitative Structure Activity Analysis (QSAR) modeling data were used to assess the environmental fate of the chemicals of interest. The QSAR analysis was conducted using the US Environmental Protection Agency's computer program, EPI (Estimation Program Interface) Suite^{TM}. Data from literature and EPI Suite were evaluated to estimate each chemicals likely behavior in the environment and to assess the uncertainty of EPI Suite model output.

From the screening level analysis, it appears as if the compounds of interest may have some characteristics that are similar to AP from an environmental fate and transport perspective. However, it is possible that two of the compounds, HCO and DNNC, are much less soluble in water when compared to AP, which would reduce the likelihood of environmental transport for these two chemicals. Additionally, it is anticipated that all of the compounds of interest will readily photodegrade. However, rates of degradation in subsurface soil, groundwater, deep surface water and sediment appear highly variable and may be dependent on covariables not evaluated for this assessment.

Because of the uncertainty around the modeled results, recommendations for additional analysis are provided, which could yield compound-specific data and reduce uncertainty. Our recommendations for additional investigation are summarized below.

- We recommended that additional analyses examining the impact of changing the parameter values that remained fixed in the initial assessment as well as evaluating the individual programs and their respective outputs when the programs are not utilized as a subroutine for the EPI Suite program be undertaken.

- We recommended that laboratory testing be considered for the determination of the most important parameters affecting fate and transport in the environment (water solubility, K_{ow}, etc).

- Finally, it is recommended that a protocol be developed that systematically describes the steps that should be followed when evaluating new energetic chemicals from an environmental liability standpoint

1.0 INTRODUCTION

The military is continuously researching and developing improved replacement propellants and explosive materials for use in munitions. Chemical propellants and explosives can undergo research and development for years. During these periods, they are tested for a variety of chemical and physical properties related to their suitability for use in munitions. Moreover, at any one time there can be numerous chemicals in various stages of development. Significant personnel as well as financial resources are dedicated to the development of these chemicals. Identification of less suitable chemicals or ones that carry additional environmental liability early in the development process aids in focusing resources on those chemicals with maximum application potential and minimal environmental liability.

Historically, the evaluation of success or failure of these chemicals has focused on their performance as propellants and/or explosives, whereas little attention has been paid to the potential environmental liability. More recently, environmental mobility, persistence and potential toxicity issues related to perchlorate have highlighted the importance of trying to anticipate the environmental risk before beginning large-scale production of a new oxidizer. In other words, assessment of the environmental impact needs to be performed before embarking on an expensive synthesis effort.

Recognizing this, the Naval Surface Warfare Center (NSWC) contracted with AMEC Earth and Environmental (AMEC) to estimate the fate-and-transport and toxicological properties of new oxidizers proposed to replace perchlorate in rocket propellant formulations. AMEC's predictive assessment uses a uniquely defined architecture to evaluate whether the new oxidizers proposed to replace perchlorate are more or less environmentally benign relative to perchlorate.

NSWC has identified four energetic chemicals that are being considered for future use. These include the inorganic oxidizer ammonium di (nitramido) amine (ADNA) whose chemical structure is presented in Figure 1; the cyclic nitramine/gem-dinitro compound 1,3,5,5-tetranitrohexahydropyrimidine (DNNC) whose chemical structure is presented in Figure 2; and 1,3,3,5,7,7-hexanitro-1,5-diazacyclooctane (HCO) whose chemical structure is presented in Figure 3; and diammonium di(nitramido) dinitroethylene (ADNDNE) whose chemical structure is presented in Figure 4[1].

This report describes the methods used to estimate fate, transport, and toxicological information on the four subject chemicals (Section 2.0); discusses the findings in terms of the estimated fate, transport, and toxicity with respect to ammonium perchlorate and presents the uncertainties associated with this analysis (Section 4.0); presents a discussion of the findings (Section 5.0); and provides conclusions and recommendations (Section 6.0).
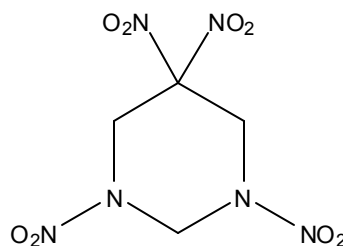
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[1] The EPI Suite model is unable to evaluate ionic bonds such as those found in ADNA. AMEC used a surrogate for ADNA, which can be viewed in Figure 5.
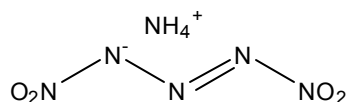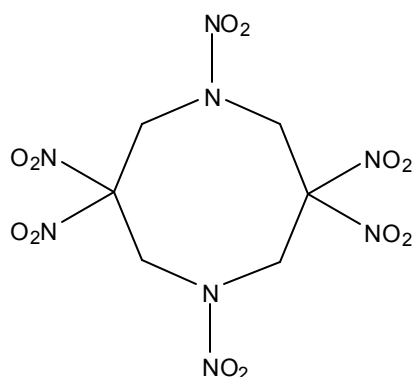
ρ = 1.76 g/mL (calc)

ΔHf = +43 kcal/mole (calc)

Figure 1. ADNA

ρ = 1.82 g/mL
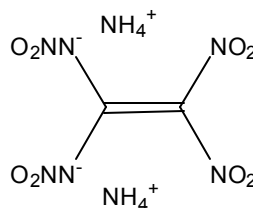
ΔHf = +11 kcal/mole

mp = 151-4 degrees C

Figure 2. DNNC

ρ = 1.875 g/mL

ΔHf = -6.52 kcal/mole

mp = 250 degrees C (dec)

Figure 3. HCO

ρ = 1.77 g/mL (calc)

ΔHf = 4.02 kcal/mole (calc)

Figure 4. ADNDNE

2.0 OBJECTIVES

The following approach was used for assessing the fate, transport, and aquatic toxicity of oxidizers early in their development. Data was generated for four oxidizers under development so that they can be ranked against perchlorate in terms of their fate, transport, and toxic properties. The priority concern is the release of potentially toxic compounds into groundwater during the use of ordnance for testing and training at military bases. Therefore, exposure is primarily going to be determined by the chemicals propensity to disperse in the environment, i.e. to contaminate soil and quickly migrate to surface water or groundwater.

Task 1: Conduct a literature search to obtain any relevant information on fundamental properties that affect fate, transport, and toxicity on the four proposed compounds. If data on the primary oxidizer is not available, a literature search will be conducted for surrogate chemicals (i.e., chemicals that have similar chemical structures and may behave similar to the oxidizer being considered).

Task 2: Conduct an initial screening and ranking using selected environmental software QSAR models (e.g., EPIWIN, ECOSAR) that predict physicochemical properties of a chemical, disposition in various environmental media, and subsequent toxicity should receptor exposure occur. These models work by comparing the structure of the oxidizer in question to large chemical libraries containing thousands of similar compounds that already have known environmental properties. These properties are further regressed against known environmental behavior endpoints, such as persistence, bioaccumulation and toxicity. The model output provides a reasonably accurate assessment of how the chemical might partition to air, water, soil and sediment if it were to be introduced into the general environment.

Some of the predictive output parameters will be the octanol-water partition coefficient (K_{ow}), water solubility, Henry's Law Constant, propensity to biodegrade, half-life in air, soil adsorption coefficient, and half-life in surface water. Those chemicals that rank lowest for potential environmental mobility and toxicity will be subject to fugacity modeling to estimate equilibrium concentrations in various environmental compartments (assuming a known flux to soil, air, water, sediment, and biota).

The data generated from the literature review and the QSAR modeling will be used to rank the new compounds against perchlorate from a fate-and-transport/toxicology prospective. The comparative ranking will be limited to the data generated as part of the literature review and QSAR modeling. It's important to note that this screening-level analysis will not allow for a comparison of all physiochemical and toxicological properties that are known for perchlorate. For example, it is likely that studies of subtle chronic health effects of the proposed oxidizers will not be available, nor is this information generated as part of the proposed QSAR modeling. In contrast, data on subtle chronic health effects for perchlorate are available. As a result of the incomplete datasets, a comparison of chronic health effects will not be possible. Nevertheless, the data that are generated and used for the comparison are significant in their ability to assess the environmental viability of the proposed oxidizers with respect to perchlorate.

3.0 METHODS

The methods used in the assessment include the following:

1. Literature search to develop a database of known physical and chemical characteristics for each of the subject chemicals;
2. Screening evaluation of each chemical using a Quantitative Structure Activity Analysis (QSAR) approach to estimate physical and chemical data that are not known or found in the literature; and
3. Evaluate the uncertainty in the QSAR analysis by evaluating similar surrogate chemicals with measured and published physical and chemical data.

Each of these steps is detailed below.

3.1 Literature Search

AMEC conducted DIALOG database and Internet literature searches to obtain relevant information on fundamental properties affecting the fate, transport, and toxicity on the four proposed compounds and other surrogate compounds. DIALOG is a collection of millions of documents drawn from more sources than any other online searchable database service. In addition, data for structurally similar compounds were obtained as part of the literature search. The DIALOG databases searched include:

1. INSPEC - The Database for Physics, Electronics and Computing (1969-present)
2. NTIS – National Technical Information System
3. Ei Compendex - worldwide coverage of approximately 4,500 journals and selected government reports and books,
4. Science Search - an international, multidisciplinary index to the literature of science, technology, biomedicine, and related disciplines (1991-present)
5. Energy Science Technology – (formerly DOE ENERGY) is a multidisciplinary file containing worldwide references to basic and applied scientific and technical research literature (1976-present),
6. Wilson Applied Science & Technology Abstracts. - provides comprehensive abstracting and indexing of more than 400 core English-language scientific and technical publications,
7. Chapman & Hall Chemical Database (CHCD) – (formerly HEILBRON) the chemical properties database, represents the complete text of several chemical dictionaries from Chapman and Hall,
8. Chemical Engineering and Biotechnology Abstracts (CEABA) - this database corresponds to the printed publications *Chemical Engineering* and *Biotechnology Abstracts.*

In addition to the Dialog search, AMEC searched the Internet and publicly available databases such as Storming Media. AMEC also searched for relevant sources of information in our internal library, which contains the majority of the published literature on the environmental and toxicological properties of the explosives and propellants in production by the US military. Technical reports and journal articles that were deemed to be relevant to this project were retrieved and reviewed. A bibliography of the literature secured by AMEC is presented in Appendix A.

The data collected as part of the literature search and review effort are used as initial input into the QSAR computer program discussed below. Despite finding a large number of technically relevant materials in the literature search, little empirical data was available for the subject compounds ADNA, DNNC, HCO, and ADNDNE. Appendix B summarizes the data found in the literature on these compounds.

3.2 EPI Suite

EPI (Estimation Program Interface) Suite^{TM} is a publicly available Windows® based suite of physical/chemical property and environmental fate estimation models developed by the US Environmental Protection Agency (EPA). EPI Suite is comprised of individual chemical/physical estimating modules; each designed to estimate a specific physical or chemical property of a

given structure. EPI Suite is scheduled for an EPA Science Advisory Board review in late 2004 or early 2005. The model is comprised of the following modules:

- KOWWIN: Estimates the log octanol-water partition coefficient, log K_{ow}, of chemicals using an atom/fragment contribution method;
- AOPWIN: Estimates the gas-phase reaction rate for the reaction between the most prevalent atmospheric oxidant, hydroxyl radicals, and a chemical. Gas-phase ozone radical reaction rates are also estimated for olefins and acetylenes. In addition, AOPWIN informs the user if nitrate radical reaction will be important. Atmospheric half-lives for each chemical are automatically calculated using assumed average hydroxyl radical and ozone concentrations;
- HENRYWIN: Calculates the Henry's Law constant (air/water partition coefficient) using both the group contribution and the bond contribution methods;
- MPBPWIN: Melting point, boiling point, and vapor pressure of organic chemicals are estimated using a combination of techniques;
- BIOWIN: Estimates aerobic biodegradability of organic chemicals using six different models; two of these are the original Biodegradation Probability Program (BPP);
- PCKOCWIN: The ability of a chemical to sorb to soil and sediment, its soil adsorption coefficient (K_{oc}), is estimated by this program. EPI's K_{oc} estimations are based on the Sabljic molecular connectivity method with improved correction factors;
- WSKOWWIN: Estimates an octanol-water partition coefficient using the algorithms in the KOWWIN program and estimates a chemical's water solubility from this value. This method uses correction factors to modify the water solubility estimate based on regression against log K_{ow};
- HYDROWIN: Acid- and base-catalyzed hydrolysis constants for specific organic classes are estimated by HYDROWIN. A chemical's hydrolytic half-life under typical environmental conditions is also determined. Neutral hydrolysis rates are currently not estimated;
- BCFWIN: This program calculates the BioConcentration Factor and its logarithm from the log K_{ow}. The methodology is analogous to that for WSKOWWIN. Both are based on log K_{ow} and correction factors;
- WVOLWIN: Estimates the rate of volatilization of a chemical from rivers and lakes; calculates the half-life for these two processes from their rates. The model makes certain default assumptions such as water body depth, wind velocity, etc;
- STPWIN: Using several outputs from EPIWIN, this program predicts the removal of a chemical in a Sewage Treatment Plant; values are given for the total removal and three contributing processes (biodegradation, sorption to sludge, and stripping to air.) for a standard system and set of operating conditions; and
- LEV3EPI: This level III fugacity model predicts partitioning of chemicals between air, soil, sediment, and water under steady state conditions for a default model "environment"; various defaults can be changed by the user.
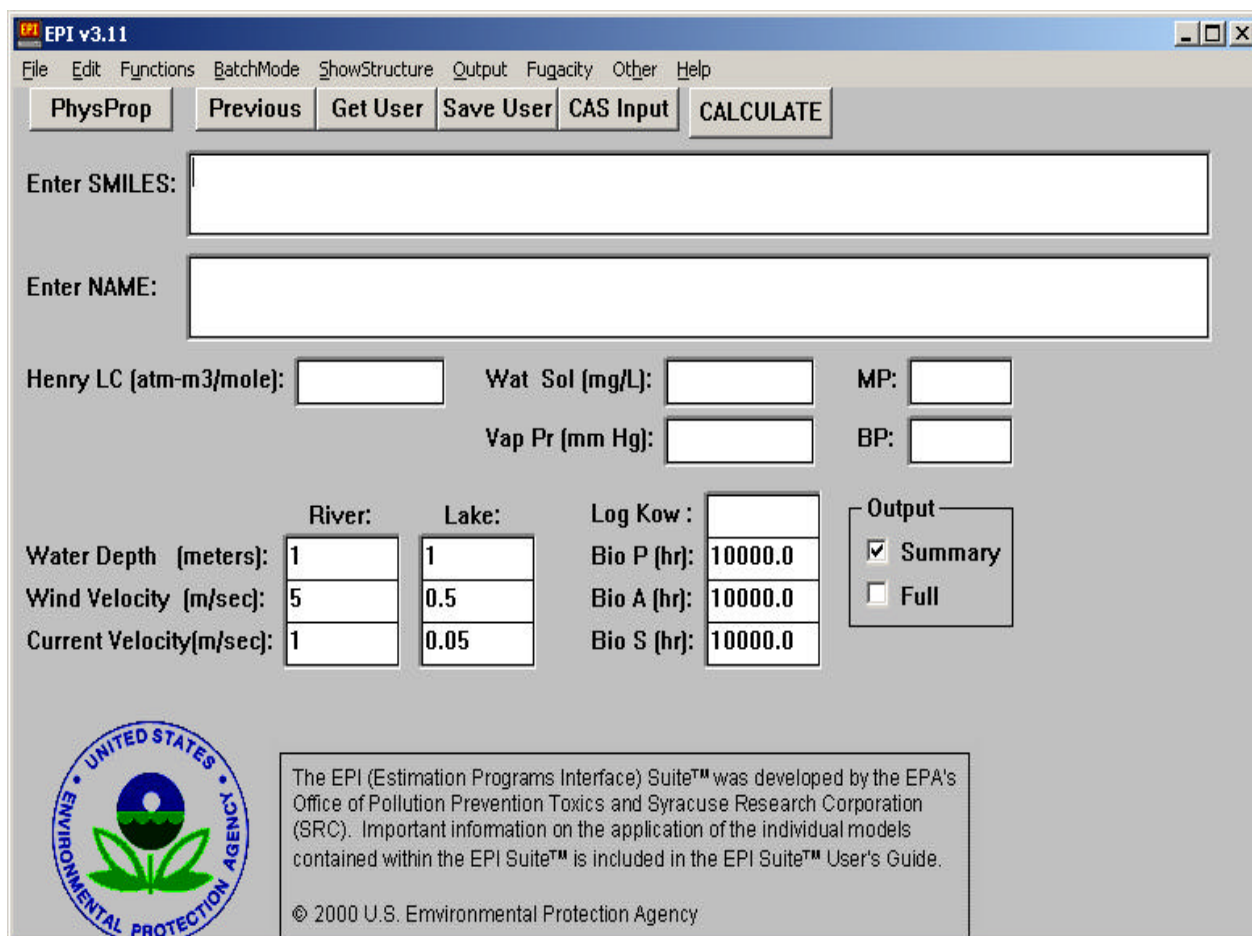
EPI Suite runs from a single input (i.e., the chemical structure in SMILES notation). SMILES is an acronym for Simplified Molecular Input Line Entry System. The notation can be created and pasted into the input screen or obtained from a linked file of CAS numbers.

The EPI Suite Interface screen has locations where additional empirically derived physical data may be entered into the program as can be seen in the diagram that follows. Data from the

literature that were available for the compounds of interest were entered into the program in a systematic way to determine their relative impacts on the program outputs. Several model runs were performed for each compound when empirical data were available, they included:

- SMILES notation as the only input with the output file labeled No_Input,
- SMILES notation plus the melting point (MP) as input with the output file labeled _MP,
- SMILES notation plus the MP & water solubility (WS) as input with the output labeled _WS
- SMILES notation plus the MP, WS, Henry's Law Constant (HLC) as input with the output labeled _HLC,
- SMILES notation plus the MP, WS, HLC, and vapor pressure (VP) as input with the output labeled _VP,
- SMILES notation plus the MP, WS, HLC, VP, and logarithm of the octanol-water partition coefficient (Log K_{ow}) as input with the output labeled _K_{ow}.

The model run outputs (full) were saved electronically as well as printed. The data were then transferred to spreadsheets for further evaluations, comparisons, and chart production.


Little empirically derived physical/chemical data were available for the four compounds of interest. Nevertheless, using the chemical structures, EPI Suite estimated the chemical

properties of the four chemicals. The estimated chemical properties from EPI Suite may provide adequate information for ranking the proposed chemicals in terms of their environmental mobility, persistence/bioaccumulation, and toxicity. However, it is also possible the estimates from EPI Suite may not adequately describe the compounds of interest. Because there are very few empirically derived data for these chemicals, it is not possible to "ground truth" the EPI Suite output for these chemicals.

In an effort to ground truth the EPI Suite model, an indirect method was employed evaluating four compounds analogous to the compounds of interest, but for which there are known chemical/physical properties. Analogue compounds were selected resembling the chemical structure of the four compounds of interest. Specifically, ammonium dinitramide (ADN) was an analogue used for ADNA; hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX) was an analogue for DNNC; octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX) was an analogue for HCO; and 1,1-diamino-2,2-dinitroethene (FOX-7) was an analogue for ADNDNE. The chemical structures that follow are included to permit visual comparisons of the compounds and their respective analogues.

Figure 5. Compounds of interest and their analogues.
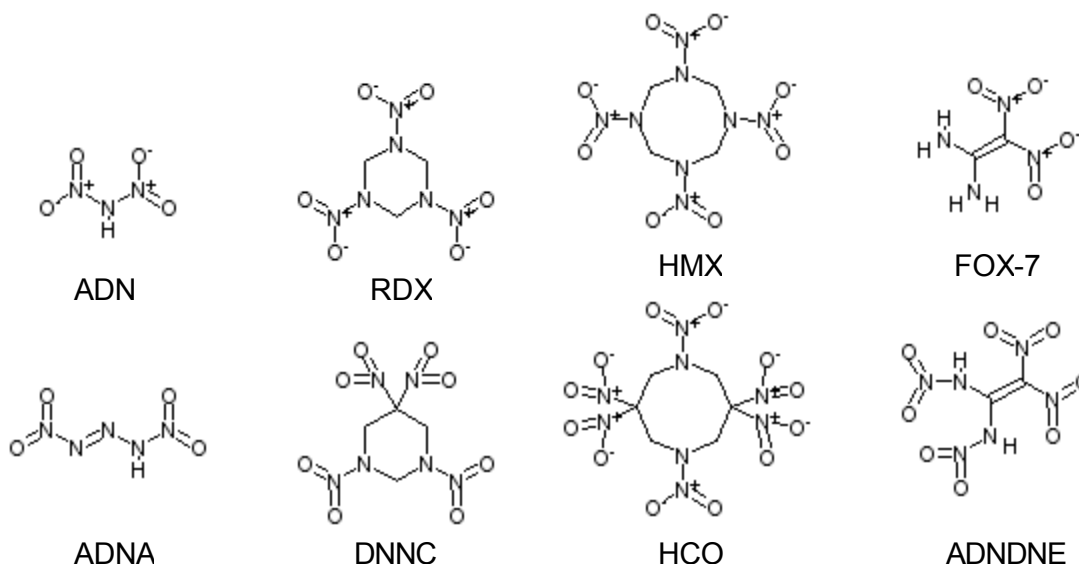
The initial examination of the compounds of interest using the EPI Suite software included adding a variety of physical and chemical input parameter values. The parameters selected to have additional value inputs were accessible on the top portion of the EPI Suite interface and include melting point, water solubility, Henry's Law Constant, vapor pressure, and the logarithm of the octanol-water partition coefficient. These data were entered into the interface when literature values were available. Other parameter value changes and methods of input remain to be examined to further refine and evaluate the proposed methodology.

Finally, in addition to the chemicals of interest and their analogs, AMEC ran ammonium perchlorate (AP) through the EPI Suite software. The data for AP is used as a basis of

comparison for the compounds of interest. The data for mobility, bioaccumulation, and toxicity for the compounds of interest are compared to that of AP.

The SMILES notations that follow were developed for the eight compounds and ammonium perchlorate (AP).

Table 1. Summary of SMILES Notations for the compounds of interest.

ADN	O=[N+]([O-])N[N+]([O-])=O
ADNA	O=[N+]([O-])N\N=N\[N+]([O-])=O
RDX	O=[N+]([O-])N1CN([N+]([O-])=O)CN([N+]([O-])=O)C1
DNNC	O=[N+]([O-])C1([N+]([O-])=O)CN([N+]([O-])=O)CN([N+]([O-])=O)C1
HMX	O=[N+]([O-])N1CN([N+]([O-])=O)CN([N+]([O-])=O)CN([N+]([O-])=O)C1
HCO	O=[N+]([O-])C1([N+]([O-])=O)CN([N+]([O-])=O)CC([N+]([O-])=O)([N+]([O-])=O)CN([N+]([O-])=O)C1
FOX-7	N/C(N)=C([N+]([O-])=O)\[N+]([O-])=O
ADNDNE	O=[N+]([O-])/C([N+]([O-])=O)=C(N[N+]([O-])=O)\N[N+]([O-])=O
AP	O=Cl(=O)(=O)ON(H)(H)(H)H

The SMILES notation for each compound was input into EPI Suite utilizing the sequence described above. For two of the compounds, ADNA and ADNDNE, no empirical physical/chemical data were found in the literature reviewed. For the other compounds limited chemical/physical data were found; in some cases being limited to the melting point (MP). For ADNA and ADNDNE, EPI Suite was run using the SMILES notation as the sole input. For the other compounds, EPI Suite was run iteratively with all other available literature-derived data as input. However, a systematic evaluation of the effect of EPI Suite inputs on model estimate outputs indicated melting point and K_{ow} were the parameters that, if included as model input, resulted in the greatest effect on model output when compared to the model output using SMILES notation as the sole input. As a result, the analysis presented herein reports and compares the EPI Suite model output when run using the following as model inputs:

1. the SMILES notation alone;
2. the SMILES notation and melting point together;
3. and the SMILES notation, the melting point and the $K_{ow.}$

As mentioned above, the empirically derived melting point and/or K_{ow} were not available for all chemicals. As a result, in some cases the model input iterations were limited by the availability of data from the literature.

Where available, the EPI Suite output from these modeling runs is compared to its respective empirically based literature value(s). In addition, the modeled data generated for the compounds of interest are contrasted with data generated for their respective analogs. Finally, the information known or estimated for AP is contrasted with the compounds of interest.

4.0 FINDINGS

Data summaries are presented from the EPI Suite model runs for both the compounds of interest and the analogue compounds. The following sections display summaries of the

empirical data and EPI Suite results for each compound of interest (e.g., ADNA). Following the display of data for the compound of interest, a similar display of data is provided for its analogue compound (e.g., ADN for ADNA). Shading in the tables highlights where model output changed based on input. Evaluations of the EPI Suite outputs for the compound of interest and analogue follow the data summaries.

4.1   ADNA and Its Analogue ADN

Summaries of the modeling output for ADNA and ADN are included in this Section[2]. Table 2 summarizes the literature data and the EPI Suite output for ADNA. Table 3 summarizes the literature and EPI Suite data for ADN.

The EPI Suite generated data for ADNA is based on the SMILES input alone (see Table 2). The results of the EPI Suites modeling indicate that ADNA is hydrophilic and highly water soluble (115,600 mg/L). Accordingly, EPI Suites data suggest that ADNA is not likely to bioaccumulate. This is indicated by the relatively low estimated log K_{ow} (-0.14) and organic carbon partition coefficient (K_{oc} = 3.359) which is indicative of a compound that is not likely to partition into lipids. Log K_{ow} values are also directly proportional to aquatic toxicity, and values less than 1 will not generally pose a problem to fish and wildlife. As such, ADNA is not likely to pose a hazard to aquatic biota nor biomagnify in the food chain. However, the estimated value for K_{oc} also suggests that ADNA will not sorb strongly to organic material in soils and other media.

The estimated vapor pressure and Henry's Law constants for ADNA are very low, indicating volatilization is not a likely transport pathway. The estimated half-life for ADNA in air (100,000 hrs) is based on hydrolysis and does not consider photolysis. However, others have suggested that ADN has a photolysis half-life on the order of minutes (Mill and Spanggord, 1997). Given the similar structures of ADNA and ADN, ADNA will likely photodegrade quickly as well.
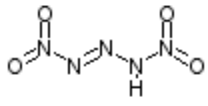
The estimates of half-life in water and soil (360 hrs each) are indicative of a compound that will degrade relatively slowly in the environment. At the surface of the soil or in the top of the water column, ADNA will likely degrade more quickly via photolysis than suggested by the model results for these media. However, for groundwater, subsurface soil, and deeper surface water (>1m) the rate of degradation will likely be markedly slower.

Table 3 summarizes the literature and EPI Suite output for the ADNA analogue, ADN. The empirically derived melting point for ADN is 92 ^{o}C, and contrasts rather sharply with the melting point predicted with EPI Suite, 245.66 ^{o}C. However, empirical and modeled values for water solubility and vapor pressure were generally in agreement. Both the literature value and the EPI Suite model output for water solubility, 500,000 and 1,000,000 mg/l, respectively, are indicative of a very highly water soluble chemical. Similarly, the literature and EPI Suite values for vapor pressure are in agreement in that they both suggest that ADN is not readily volatilized under environmental conditions. The literature half-life values for water are very different from those

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[2] The EPI Suite model is unable to evaluate ionic bonds such as those found in ADNA. AMEC used a surrogate for ADNA, which can be viewed in Figure 5.

Table 2. Summary of ADNA literature values and EPI Suite input and output.

EPI Suite Output	ADNA			
	Ammonium di(nitramido)amine			
Molecular Formula	$H_1 N_5 O_4$			
Molecular Weight (g/mol)	135.04			
		EPI Suite Input		
	Literature Value	SMILES Only	SMILES & MP	SMILES, MP & K_{ow}
Physical State				
Melting Point (^{o}C)	NA [a]	273.11	Not run [b]	Not run
Boiling Point (^{o}C)	NA	629.53	Not run	Not run
Solubility, Water (mg/L)	NA	115600	Not run	Not run
Partition Coefficients				
Log K_{ow}	NA	-0.14	Not run	Not run
K_{oc}	NA	3.359	Not run	Not run
Vapor Pressure (mm Hg at 25°C)	NA	2.30E-14	Not run	Not run
Henry's Law Constant (atm-m^3/mole)	NA	7.45E-09	Not run	Not run
Half-life in Air (hr)	NA	100000	Not run	Not run
Half-life in Water (hr)	NA	360	Not run	Not run
Half-life in Soil (hr)	NA	360	Not run	Not run
Half-life in Sediment (hr)	NA	1440	Not run	Not run
Daphnid LC50 (mg/L)	NA	9502	Not run	Not run
LOEC (Daphnid EC50) (mg/L)	NA	191	Not run	Not run
Chemical Structure				
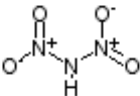
Notes:
a – NA = Not available in researched literature.
b – These iterations were not run in EPI Suites because empirical literature data were not found for melting point and/or K_{ow}.
MP – melting point.

Table 3. Summary of ADN literature values and EPI Suite input and output.

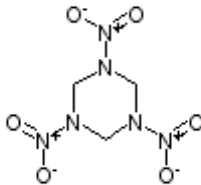| EPI Suite Output	ADN		
	Ammonium dinitramide		
Molecular Formula	$H_4N_4O_4$		
Molecular Weight (g/mol)	124.06		
		EPI Suite Input	
	Literature Value	SMILES Only	SMILES & MP	SMILES, MP & K_{ow}
Physical State	Solid			
Melting Point (^{o}C)	92[a]	245.66	245.66	Not run [c]
Boiling Point (^{o}C)	NA[b]	570.78	570.78	Not run
Solubility, Water (mg/L)	500,000[a]	1.00E+06	1.00E+06	Not run
Partition Coefficients				
Log K_{ow}	NA	-1.29	-1.29	Not run
K_{cc}	NA	10.53	10.53	Not run
Vapor Pressure (mm Hg at 25°C)	~0	1.71E-12	9.56E-11	Not run
Henry's Law Constant (atm-m^3/mole)	NA	1.27E-07	1.27E-07	Not run
Half-life in Air (hr)	NA	100000	100000	Not run
Half-life in Water (hr)	370 yrs[a]	360	360	Not run
Half-life in Soil (hr)	NA	360	360	Not run
Half-life in Sediment (hr)	NA	1440	1440	Not run
Daphnid LC50 (mg/L)	NA	83827.813	83827.81	Not run
LOEC (Daphnid EC50) (mg/L)	NA	1019.267	1019.267	Not run
Chemical Structure			

Notes:
a – Mill and Spanggord, 1997.
b – NA = Not available in researched literature.
c – These iterations were not run in EPI Suites because empirical literature data were not found for melting point and/or K_{ow}.
MP – melting point.

that are estimated from EPI Suite (370 yrs vs. 360 hrs, respectively). The reason for this discrepancy between the empirical and modeled data is unclear, but Mill and Spanggord (1997) state ADN is hydrolytically stable in water at environmentally relevant pHs at 25 $^{\circ}$C. In addition, Mill and Spanggord (1997) state that biotransformation of ADN in soil and water, under aerobic and anaerobic conditions was not observed although it did degrade when a glucose substrate was added. However, as mentioned above, ADN has been demonstrated to photolyze very rapidly. Finally, ADN is also estimated to have relatively low log K_{ow}, indicating it is not highly lipophilic and not likely to bioaccumulate. Log K_{ow} values are also directly proportional to aquatic toxicity, and values less than 1 will not generally pose a problem to fish and wildlife. As such, ADNA is not likely to pose a hazard to aquatic biota.

Taken together, the predicted high water solubility, low predicted K_{oc}, the relatively long half-lives for ADNA in soil and water, and the suggested evidence from ADN's recalcitrant nature in soil and water indicate that ADNA, if introduced to the environment, would be readily mobilized by water (percolation through the vadose zone, groundwater, and/or surface water). To the extent that ADNA is on the soil surface or near the top of the surface water column, photodegradation may play an important role in naturally attenuating concentrations of ADNA. However, once below the ground surface, in groundwater, or otherwise in a location without adequate sunlight, little decomposition via abiotic pathways may occur.

4.2   DNNC and Its Analogue RDX

Table 4 summarizes the empirical and EPI Suite outputs for DNNC. As shown in Table 4, literature values for the melting point for DNNC were available, and ranged from 151 to 154 $^{\circ}$C. EPI Suite estimate the melting point for DNNC to be 148.46 $^{\circ}$C using only the SMILES format as model input. For DNNC, the empirical and modeled melting points are in good agreement.
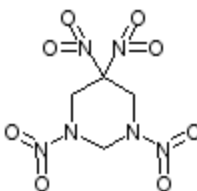
EPI Suite model output for DNNC water solubility ranges from 73,140 mg/L when using the SMILES notation alone to 50,100 mg/L when using both the SMILES notation and the literature value for melting point. Although there is a difference in predicted water solubility for the two EPI Suite model runs, the differences are relatively small, and both indicate DNNC is a relatively highly water soluble chemical. However, of the four compounds of interest evaluated here, DNNC is predicted to be the least soluble.

The predicted log K_{ow} for DNNC, -1.14, indicates this compound in not lipophilic and thus will not readily bioaccumulate and biomagnify in the food chain. Because low K_{ow}'s are also indicative of low aquatic toxicity, this compound is not expected to pose a hazard to freshwater fish or macroinvertebrates. The predicted K_{oc} for DNNC is higher than predicted for ADNA, suggesting it may have a lower propensity for movement in soil and may sorb to soil and sediment more readily than ADNA. The predicted K_{oc} for DNNC is similar to some semi volatile compounds such as naphthalene and dibenzofuran.

Like ADNA, DNNC is not likely to volatilize to the atmosphere once released to the environment. This is suggested from the very low predicted vapor pressures and Henry's law constant. Nevertheless, if DNNC were to be released to the air, EPI Suite predicts a very rapid half-life in air, 3 hrs, so its residence time and transport in the atmosphere may be limited.

The predicted half-lives in the other environmental compartments, water, soil and sediment, are similar in magnitude to those predicted for ADNA and ADN.

Table 4. Summary of DNNC literature values and EPI Suite input and output.

EPI Suite Output	DNNC or TNDA			
	1,3,5,5-Tetranitrohexahydropyrimidine			
Molecular Formula	$C_4H_6N_6O_8$			
Molecular Weight (g/mol)	266.13			
		EPI Suite Input		
	Literature Value	SMILES Only	SMILES & MP	SMILES, MP & K_{ow}
Physical State				
Melting Point (^{o}C)	151 - 154[a]	148.46	148.46	Not run[c]
Boiling Point (^{o}C)	NA[b]	397.67	397.67	Not run
Solubility, Water (mg/L)	NA	73140	50100	Not run
Partition Coefficients				
Log K_{ow}	NA	-1.14	-1.14	Not run
K_{oc}	NA	1678	1678	Not run
Vapor Pressure (mm Hg at 25°C)	NA	5.27E-07	4.81E-07	Not run
Henry's Law Constant (atm-m^3/mole)	NA	8.39E-15	8.39E-15	Not run
Half-life in Air (hr)	NA	3	3	Not run
Half-life in Water (hr)	NA	900	900	Not run
Half-life in Soil (hr)	NA	900	900	Not run
Half-life in Sediment (hr)	NA	3600	3600	Not run
Daphnid LC50 (mg/L)	NA	152000	152000	Not run
LOEC (Daphnid EC50) (mg/L)	NA	1976	1976	Not run
Chemical Structure				

Notes:
a – Oyumi and Brill, 1985
b - NA = Not available in researched literature.
c – These iterations were not run in EPI Suites because empirical literature data were not found for melting point and/or K_{ow}.
MP – melting point.

Table 5. Summary of RDX literature values and EPI Suite input and output.

EPI Suite Output	RDX Hexahydro-1,3,5-trinitro-1,3,5-triazine			
Molecular Formula	$C_3H_6N_6O_6$			
Molecular Weight (g/mol)	222.12			
		EPI Suite Input		
	Literature Value	SMILES Only	SMILES & MP	SMILES, MP & K_{ow}
Physical State	Crystalline Solid			
Melting Point (^{o}C)	204 - 206[a]	132.76	132.76	132.76
Boiling Point (^{o}C)	NA[b]	353.43	353.43	353.43
Solubility, Water (mg/L)	59.9[a]	6062	709.5	611.8
Partition Coefficients				
Log K_{ow}	0.937[a]	0.68	0.68	0.68
K_{oc}	1.86[a]	195	195	195
Vapor Pressure (mm Hg at 25°C)	2.00E-09[a]	1.32E-06	1.36E-06	1.36E-06
Henry's Law Constant (atm-m^3/mole)	1.95E-11[a]	6.32E-08	6.32E-08	6.32E-08
Half-life in Air (hr)	10.7 - 168[c]	1.043	1.043	1.043
Half-life in Water (hr)	75 - 2.2E08[d]	900	900	900
Half-life in Soil (hr)	323 - 6E07[e]	900	900	900
Half-life in Sediment (hr)	NA	3600	3600	3600
Daphnid LC50 (mg/L)	NA	2804	2804	1636.49
LOEC (Daphnid EC50) (mg/L)	NA	80.72	80.72	52.716
Chemical Structure				

Notes:

a - Meyer, 1977.

b - NA = Not available in researched literature.

c - Sikka et al. 1990, Spanggord et al.1978.

d - Price et al. 1998, Spanggord et al. 1980.

e - Pennington et al. 2001, Deliman & Gerald, 1998.

MP – melting point.

Table 5 summarizes the literature derived and EPI Suite values for RDX. In this case, EPI Suite under predicted the melting point of RDX by 60 percent. In contrast, EPI Suite over predicted the water solubility of RDX by as much as two orders of magnitude when the EPI Suite input was limited to the SMILES notation, and by a single order of magnitude when the melting point and/or K_{ow} are input to the model. The contrast between the relatively low water solubility for RDX from the literature, 59.9 mg/L, and that predicted for DNNC; 50,100 to 73,140 mg/L, may be explained by the increased number of oxygen's present on DNNC. The increased oxygen content of the molecule may allow for additional hydrogen bonding, which could result in higher water solubility. However, it is also possible that the EPI Suites model is over predicting the DNNC water solubility in the same way that it is over predicting RDX water solubility.

The literature and predicted log K_{ow} for RDX are in good agreement. However, a two order of magnitude difference is seen between the literature and predicted K_{oc} for RDX. The difference between the literature and predicted K_{oc} for RDX, may suggest the predicted K_{oc} for DNNC is overestimated. If this is the case, DNNC may be more mobile in soil, groundwater, and sediment than one might deduce from the EPI Suites predicted K_{oc} by itself.

The vapor pressures and Henry's law constant for RDX predicted by EPI Suite are several orders of magnitude greater than those found in the literature. However, from an environmental fate and transport perspective, RDX would not be considered a volatile chemical regardless of which values (literature or predicted) were used. Both values suggest that RDX exposed to the air or dissolved in water would not readily volatilize into the atmosphere.

Predicted half-lives in the four environmental compartments are nearly identical for RDX and DNNC, suggesting their persistence in the environment may be similar. RDX's presence has been documented in the groundwater at a number of manufacturing and military installations.

4.3   HCO and Its Analogue HMX

Table 6 summarizes the literature values and EPI Suite output for the compound of interest, HCO. Like DNNC, an empirically derived melting point value for HCO was available from the literature (250 °C). Using the SMILES notation alone, EPI Suite computed a melting point of 221.47 °C, which is in good agreement with the empirically derived value.

EPI Suite model output for HCO water solubility ranges from 384,100 mg/L when using the SMILES notation alone to 153,000 mg/L when using both the SMILES notation and the literature value for melting point. Although there is a difference in predicted water solubility for the two EPI Suite model runs, the difference is only a factor of 2.5. Nevertheless, both values for predicted water solubility indicate HCO is a relatively highly water soluble chemical.

The predicted log K_{ow} for HCO, -2.28, indicates that this compound in not lipophilic and thus will not readily bioaccumulate and/or biomagnify in the foodchain. Low log K_{ow}'s are also indicative of a low potential to pose a hazard to freshwater fish and wildlife. The predicted K_{oc} for HCO, 136,700, is the highest predicted for all of the compounds of interest. The high K_{oc} value indicates this compound will not move through soil and may sorb to soil and sediment more readily than the other compounds of interest. The predicted K_{oc} for HCO is similar to relatively persistent compounds.

Given the predicted vapor pressure and Henry's law constant, HCO is not likely to volatilize to the atmosphere once released to the environment. The atmospheric residence time of HCO is likely to be small given the predicted half live of 48 hours.
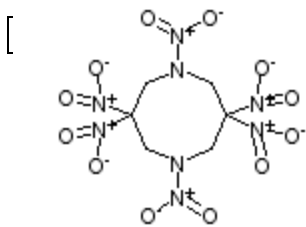
The predicted half-lives in the other environmental compartments, water, soil and sediment, are similar in magnitude to those predicted for the other compounds of interest. These results suggest that if HCO is introduced into the environment as a dissolved species it will be persistent and recalcitrant and highly mobile, similar to HMX.

Table 7 summarizes the literature derived and EPI Suite values for HMX. In this case, EPI Suite under predicted the melting point of HMX by approximately 65 percent. In contrast, EPI Suite over predicted the water solubility of HMX by as much as 2.5 orders of magnitude when the EPI

Suite input was limited to the SMILES notation, and as much as two orders of magnitude when the melting point and K_{ow} are input to the model. Similar to the comparison made above for DNNC and RDX, the contrast between the relatively low water solubility for HMX from the literature, 5 to 6.63 mg/L, and that predicted for HCO, 153,000 to 384,100 mg/L, may be explained by the increased number of oxygen's present on HCO. The increased oxygen content of the molecule may allow for additional hydrogen bonding, which could result in higher water solubility. However, it is also possible the EPI Suites model is over predicting the HCO water solubility in the same way that it is over predicting for HMX.

The literature and predicted log K_{ow} for HMX are in good agreement. However, a nearly 3.5 order of magnitude difference is seen between the literature and predicted K_{oc} for HMX. The difference between the literature and predicted K_{oc} for HMX, may suggest the predicted K_{oc} for HCO is overestimated. If this is the case, HCO may be more mobile in soil, groundwater, and sediment than one might deduce from the EPI Suites predicted K_{oc} by itself.

Table 6. Summary of HCO literature values and EPI Suite input and output.

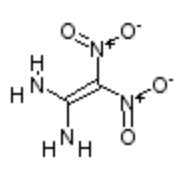| EPI Suite Output	HCO or HNDZ			
	1,3,3,5,7,7-Hexanitro-1,5-diazacyclooctane			
Molecular Formula	$C_6H_8N_8O_{12}$			
Molecular Weight (g/mol)	384.18			
		EPI Suite Input		
	Literature Value	SMILES Only	SMILES & MP	SMILES, MP & K_{ow}
Physical State				
Melting Point (^{o}C)	250[a]	221.47	221.47	Not run [c]
Boiling Point (^{o}C)	NA[b]	524.89	524.89	Not run
Solubility, Water (mg/L)	NA	384100	153000	Not run
Partition Coefficients				
Log K_{ow}	NA	-2.8	-2.8	Not run
K_{oc}	NA	136700	137000	Not run
Vapor Pressure (mm Hg at 25°C)	NA	5.08E-11	2.29E-11	Not run
Henry's Law Constant (atm-m^3/mole)	NA	1.53E-23	1.53E-23	Not run
Half-life in Air (hr)	NA	48	48	Not run
Half-life in Water (hr)	NA	1440	1440	Not run
Half-life in Soil (hr)	NA	1440	1440	Not run
Half-life in Sediment (hr)	NA	5760	5760	Not run
Daphnid LC50 (mg/L)	NA	7120000	7120000	Not run
LOEC (Daphnid EC50) (mg/L)	NA	44700	44723	Not run
Chemical Structure				
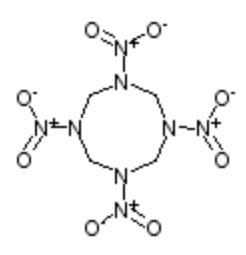
Notes:

a – Oyumi and Brill, 1985

b – NA = Not available in researched literature.

c – These iterations were not run in EPI Suites because empirical literature data were not found for melting point and/or K_{ow}.
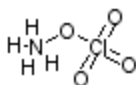
MP – melting point.

Table 7. Summary of HMX literature values and EPI Suite input and output.

EPI Suite Output	HMX Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine			
Molecular Formula	$C_4H_8N_8O_8$			
Molecular Weight (g/mol)	296.16			
			EPI Suite Input	
	Literature Value	SMILES Only	SMILES & MP	SMILES, MP & K_{ow}
Physical State	Crystalline Solid			
Melting Point (^oC)	276 - 280[a]	182.89	182.89	182.89
Boiling Point (^oC)	NA [b]	436.41	436.41	436.41
Solubility, Water (mg/L)	5 - 6.63[a]	2556	130.5	579.4
Partition Coefficients				
Log K_{ow}	0.06,0.26[a]	0.82	0.82	0.82
K_{oc}	0.54[a]	1850	1850	1850
Vapor Pressure (mm Hg at 25°C)	3.33E-14[a]	2.41E-08	1.72E-09	1.72E-09
Henry's Law Constant (atm-m^3/mole)	2.60E-15[a]	8.67E-10	8.67E-10	8.67E-10
Half-life in Air (hr)	4.6 - 168[c]	0.7819	0.7819	0.7819
Half-life in Water (hr)	11 - 425[d]	900	900	900
Half-life in Soil (hr)	3.4E05-2.8E07[e]	900	900	900
Half-life in Sediment (hr)	NA	3600	3600	3600
Daphnid LC50 (mg/L)	NA	2788.19	2788.19	11350.7
LOEC (Daphnid EC50) (mg/L)	NA	85.334	85.334	259.33
Chemical Structure				

Notes:
a - From Wildlife Toxicity Assessment for HMX.
b – NA = Not available in researched literature.
c - Bedford et al. 1996, Spanggord et al. 1983.
d - McCormick et al. 1984, Deliman & Gerald, 1998.
e - Phelan & Webb 1998, Deliman & Gerald, 1998.
MP – melting point.

4.4 ADNDNE and Its Analogue FOX-7
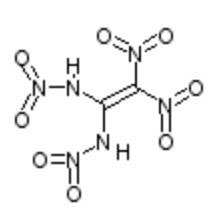
Table 8 summarizes the EPI Suite predictions for ADNDNE. No empirically derived data were found for ADNDNE in the reviewed literature. Based on the SMILES notation EPI Suite data, ADNDNE appears to be a highly water soluble chemical (232,800 mg/L). In addition, it appears from the very low predicted vapor pressures and Henry's law constants, that once in the environment, ADNDNE will not readily volatilize. Also, the predicted K_{oc}, 928, indicates ADNDNE will be moderately adsorbed by soil and sediment. Bioaccumulation and biomagnification of ADNDNE is not predicted to be significant, given the relatively low log K_{ow} of −1.54. The potential to induce adverse effects to aquatic organisms is also low because the log K_{ow} value is less than one.

Similar to the other chemicals, ADNDNE is anticipated to be quickly reduced by photolysis. Other rates for environmental degradation are less certain for water, soil and sediment, but are similar to rates predicted for the other compounds of interest.

Table 9 summarizes the literature and EPI Suite predictions for FOX-7. The only literature value found for FOX-7 was the melting point. Table 9 shows that the EPI Suite predicted melting point is less than half that reported in the literature using the SMILES notation alone. The effect on the EPI Suite output when using the literature value for the FOX-7 melting point is most notable for the estimated vapor pressure. When the literature value for melting point is used as input, the vapor pressure drops by 1.5 orders of magnitude. No other changes in EPI Suite output are noted.

Given the paucity of empirical data for both the ADNDNE and it analogue, FOX-7, there is little certainty in the EPI Suite output for these compounds.

Table 8. Summary of ADNDNE literature values and EPI Suite input and output.

EPI Suite Output	ADNDNE			
	Diammonium di(nitramido)dinitroethylene			
Molecular Formula	$C_2H_2N_6O_8$			
Molecular Weight (g/mol)	238.07			
			EPI Suite Input	
	Literature Value	SMILES Only	SMILES & MP	SMILES, MP & K_{ow}
Physical State				
Melting Point (^oC)	NA[a]	127.89	Not run [b]	Not run
Boiling Point (^oC)	NA	388.92	Not run	Not run
Solubility, Water (mg/L)	NA	232,800	Not run	Not run
Partition Coefficients				
Log K_{ow}	NA	-1.54	Not run	Not run
K_{oc}	NA	928.1	Not run	Not run
Vapor Pressure (mm Hg at 25^oC)	NA	1.45E-06	Not run	Not run
Henry's Law Constant (atm-m^3/mole)	NA	5.27E-14	Not run	Not run
Half-life in Air (hr)	NA	138	Not run	Not run
Half-life in Water (hr)	NA	900	Not run	Not run
Half-life in Soil (hr)	NA	900	Not run	Not run
Half-life in Sediment (hr)	NA	3600	Not run	Not run
Daphnid LC50 (mg/L)	NA	315,000	Not run	Not run
LOEC (Daphnid EC50) (mg/L)	NA	3430	Not run	Not run
Chemical Structure				

Notes:
a – NA = Not available in researched literature.
b – These iterations were not run in EPI Suites because empirical literature data were not found for melting point and/or K_{ow}.
MP – melting point.

Table 9. Summary of FOX-7 literature values and EPI Suite input and output.

EPI Suite Output	FOX-7		
	1,1-Diamino-2,2-dinitroethene		
Molecular Formula	$C_2H_4N_4O_4$		
Molecular Weight (g/mol)	148.08		
		EPI Suite Input	
	Literature Value	SMILES Only	SMILES & MP	SMILES, MP & K_{ow}
Physical State				
Melting Point (^oC)	205	83.37	83.37	Not run [b]
Boiling Point (^oC)	NA[a]	287.51	287.51	Not run
Solubility, Water (mg/L)	NA	1.00E+06	1.00E+06	Not run
Partion Coefficients				
Log K_{ow}	NA	-2.86	-2.86	Not run
K_{cc}	NA	30.6	30.6	Not run
Vapor Pressure (mm Hg at 25^oC)	NA	0.00104	4.70E-05	Not run
Henry's Law Constant (atm-m^3/mole)	NA	1.43E-12	1.43E-12	Not run
Half-life in Air (hr)	NA	5.85	5.85	Not run
Half-life in Water (hr)	NA	360	360	Not run
Half-life in Soil (hr)	NA	360	360	Not run
Half-life in Sediment (hr)	NA	1440	1440	Not run
Daphnid LC50 (mg/L)	NA	2073.6	2073.6	Not run
LOEC (Daphnid EC50) (mg/L)	NA	-	-	Not run
Chemical Structure			

Notes:

a – NA = Not available in researched literature.

b – These iterations were not run in EPI Suites because empirical literature data were not found for melting point and/or K_{ow}.

MP – melting point.

4.5   Ammonium Perchlorate

AP is evaluated here as a benchmark against which to gauge the other chemicals, since AP is the primary oxidizer in missiles and rockets and is being considered for replacement due to its environmental impact concerns. Table 10 summarizes the literature values and EPI Suite output for AP.

AP is a highly water soluble chemical, with an empirically derived water solubility of 200,000 mg/L. EPI Suite predicts AP to be completely miscible in water (1,000,000 mg/L).   The high solubility of AP is consistent with the fact that AP will dissociate forming a readily water soluble perchlorate anion.   Table 10 also shows that the predicted log K_{ow} is relatively low, indicating AP will not likely bioaccumulate or biomagnify within the food web. However, perchlorate has been measured in lettuce leaves and cows milk, indicating that biotransfer does occur in the environment. The low log K_{ow} (<1) is also a good predictor of a low potential to induce toxic effects on freshwater organisms. Additionally the predicted K_{oc} for AP is indicative of its inability to strongly sorb to soil and sediments.

Like the other compounds evaluated here, AP is not predicted to be readily volatilized in the environment, based on the modeled vapor pressure and Henry's law constant.   However, once in the environment, the degradation is predicted to be moderate to slow. This is suggested by the half lives in soil, sediment and water.

Table 10. Summary of AP literature values and EPI Suite input and output.

EPI Suite Output	AP		
	Ammonium Perchlorate		
Molecular Formula	NH_4ClO_4		
Molecular Weight (g/mol)	117.49		
		EPI Suite Input	
	Literature Value	SMILES Only	SMILES & MP	SMILES, MP & K_{ow}
Physical State				
Melting Point (^oC)	240	266.8	266.8	Not run [b]
Boiling Point (^oC)	NA[a]	616.04	616.04	Not run
Solubility, Water (mg/L)	200,000	1.00E+06	1.00E+06	Not run
Partition Coefficients				
Log K_{ow}	NA	-5.84	-5.84	Not run
K_{oc}	NA	96.6	96.6	Not run
Vapor Pressure (mm Hg at 25^oC)	NA	2.81E-11	1.33E-13	Not run
Henry's Law Constant (atm-m^3/mole)	NA	*4.344E-18	*2.056E-20	Not run
Half-life in Air (hr)	NA	100,000	100,000	Not run
Half-life in Water (hr)	NA	360	360	Not run
Half-life in Soil (hr)	NA	360	360	Not run
Half-life in Sediment (hr)	NA	1440	1440	Not run
Daphnid LC50 (mg/L)	NA	1.27E+09	1.27E+09	Not run
LOEC (Daphnid EC50) (mg/L)	NA	2.11E+06	2.11E+06	Not run
		*VP/WS not a bond estimate		
Chemical Structure			

Notes:

a – NA = Not available in researched literature.

b – These iterations were not run in EPI Suites because empirical literature data were not found for melting point and/or K_{ow}.

MP – melting point.

5.0 DISCUSSION OF RESULTS

The information discussed above for the chemicals of interest, their analogues and AP provides information that is used in this report to assess the potential validity of the predicted (i.e., modeled) results and to compare the fate and transport potential of the compounds of interest to that of AP. A summary of measured and model-estimated physical and chemical properties for the chemicals is provided in Appendix B. In addition, a cursory evaluation of the toxicity of these compounds is also presented. Each of these is summarized below.

5.1   EPI Suite Model Validity

Although EPI Suite is capable of producing estimates of a variety of environmentally significant physical/chemical parameters, it does have limitations. For example, Zakikhani et al. (2002) state that QSAR models such as EPI Suite can produce estimates of octanol water partition coefficients with a mean error equivalent to the experimental mean error. However, Zakikhani et al (2002) also state that improved methods are still required for estimating biodegradation rates.

In this analysis, differences between modeled and measured data are most notable for water solubility and K_{oc}. This was the case for RDX and HMX, and in both cases, EPI Suite tended to overestimate the water solubility and the K_{oc}. Given the similarities in the structures, it is possible that the water solubility and K_{oc} predicted for their analogues, DNNC and HCO are also over predicted.

Literature derived and EPI Suite generated vapor pressures differed by several orders of magnitude in some cases. However, because both the literature value and the estimated values were so low, the overall conclusion regarding the unimportance of the volatilization/air pathway is not effected.

Differences in empirically derived and modeled melting points were noted for ADN and FOX-7. However, other parameters (e.g., water solubility, and vapor pressure) did not appear significantly affected by the differing melting point estimates.

Except for estimates of K_{oc} for HMX and perhaps RDX, the EPI Suite modeled data compared relatively well with the literature values when viewed from the standpoint of determining relative fate and transport compounds. For example, even though the literature and EPI Suite predicted water solubility for HMX and RDX are significantly different, the over all conclusions reached by this assessment (i.e., these chemicals are much less soluble than the other chemical evaluated) still remains true. Viewing the output data in this way enables interpretation and use of the EPI Suite data even when the absolute accuracy of the EPI Suite output is not known.

5.2   Fate and Transport Comparison

The model estimates of high solubility and low vapor pressure, as well as screening fugacity calculations, indicate the majority of the chemicals of interest introduced to the environment, as residues on soil would end up in groundwater. This would be especially true for the ionic compounds that would, in all likelihood, readily dissolve in water. The solubility estimates for HCO and DNNC might be overestimated given that they are saturated ring structures and that

their analogue compounds demonstrated significant differences between empirical and model estimated solubility. The predicted solubility of DNNC is approximately one quarter the water solubility of AP. However, as mentioned above, the predicted DNNC water solubility may be over predicted, so the differences with AP may be even greater.

Lack of substituted halogens (e.g., chlorine) and very low K_{ow}'s (certainly less than 1) strongly suggest these compounds would not bioconcentrate, bioaccumulate, or biomagnify in fish and/or wildlife. This it true for the compounds of interest as well as for AP[3]. The low K_{ow} values may not preclude biotransfer from the environment to biota, but will likely diminish the potential for lipophilic biomagnification.

Similarly, the aquatic toxicity QSAR estimates from EPI Suite indicate that, at anticipated environmental concentrations (low ug/L range), these compounds would not directly pose a hazard to freshwater fish or macroinvertebrates. Based on the toxicity values predicted by EPI Suite for Daphnia species (i.e., LD_{50}'s and Lowest Observed Effect Concentrations), all of the toxic endpoints would be expected to fall in the milligram per liter range. Indeed, the lowest LD_{50} and LOEC predicted for Daphnia spp. was, respectively, 2788 and 191 mg/L. This is well outside of any concentration that might be anticipated in groundwater. However, at manufacturing facilities it is possible that ppm levels of these compounds could be found in surface water. AP has been found in surface waters near manufacturing facilities well in excess of 1000's ppm.

The half-lives in water estimated by the EPI Suite model are relatively long. The oxygen uptake rate for a mixed culture of microorganisms could provide information regarding biodegradation or inhibition. Another way to test biodegradability is by conducting bench scale tests that utilize wastewater (e.g., BOD tests). Nevertheless, the half-life estimates in soil, sediment, and water for the compounds of interest are not significantly different than those for AP indicating if released into the environment they have the potential to be highly mobile.

Although photolysis may play an important part in the removal of these munitions residues from soils, hard surfaces, or the top shallow layer of surface waters, EPI Suites does not have methods for estimating half-lives for this degradation pathway. As a result, there is a high level of uncertainty in the air half-life estimates. Even if photolysis is found to be a significant degradation pathway for these chemicals, the half-lives in groundwater and subsurface soil may still remain relatively long.

5.3 Toxicological Comparison

From the standpoint of predicting or anticipating inherent toxicity, RDX would be a good working "surrogate" for DNNC; similarly, HMX would be a good surrogate for HCO; ADN would be a fair surrogate for ADNA. Although very little toxicity data could be found, it appears that reproductive and/or carcinogenic endpoints may drive future *in vitro* or *in vivo* hazard assessments (as seen with the ADN study). Most of the these compounds, once absorbed into the body, would be anticipated to be reduced in the liver (nitrate reduction to the amino- or diamino- compound) and excreted as either the mono- or diamino-substituted derivative or further transformed to more soluble metabolites via Phase I or II enzyme systems. Because of the expected metabolic recognition via the high substitution with nitrate groups, these compounds would also not be expected (based on professional judgment) to have a very long

half-life in the body and thus the possibility of a highly idiosyncratic toxic mechanism (like AP) would also be unlikely.

6.0 CONCLUSIONS AND RECOMMENDATIONS

Taken altogether, the four compounds assessed using the EPI Suite program are predicted to have physicochemical parameters that, once released into the general environment, may favor migration to surface water or groundwater. The low lipophilic nature of these compounds, as estimated by very low predicted log Kow coefficients, also assume these compounds would not bioconcentrate into aquatic organisms, nor would they bioaccumulate or biomagnify within the food chain. Direct toxicity to aquatic organisms, as estimated by QSAR-derived aquatic toxicity endpoints, is also expected to be very low.

Preliminary calculations based on the reproductive toxicology of ADN indicate acceptable drinking water (or groundwater if potable) concentrations that range between 340 and 1,015 ug/L (depending on the use and/or conservatism of uncertainty factors).

Compared to AP, the compounds of interest are anticipated to behave similarly from an environmental fate and transport perspective. However, it is possible that two of the compounds, HCO and DNNC, are much less soluble in water when compared to AP. Additionally, it is anticipated that all of the compounds of interest will readily photodegrade. However, rates of degradation in subsurface soil, groundwater, deep surface water and sediment appear highly variable and may be dependent on covariables not evaluated for this assessment.

This assessment also suggests there is some uncertainty in several of the EPI Suite Model outputs (e.g., melting point, water solubility, K_{oc}). Given that there is no empirical data to compare modeled data against for many of the compounds of interest, the uncertainty about these factors remains unquantified. It is recommended that additional analyses examining the impact of changing the parameter values that remained fixed in the initial assessment as well as evaluating the individual programs and their respective outputs when the programs are not utilized as a subroutine for the EPI Suite program be undertaken. This recommendation includes conducting additional literature database searches for physical/chemical parameters for the compounds of interest. Specifically, additional investigation and translation of the Russian literature is recommended. In addition, a thorough evaluation of the contents of the Chemical Propulsion Information Agency at Johns Hopkins University is recommended. Finally this recommendation includes conducting additional modeling on other surrogate compounds (e.g., 2,2-dinitropropane and 2-azo-2-nitropropane).

If based on additional literature searches the database of empirically derived information for the compounds of interest remains scant, it is further recommended that laboratory testing be considered for the determination of the most important parameters affecting fate and transport in the environment (water solubility, K_{ow}, etc). This suggestion is made with the understanding that analytical methods many not be available for these chemicals. As such, analytical method development may be a necessary counterpart to this recommendation. In any case, as these compounds continue to move through the various military evaluations and closer to small-scale production, it will be important supplement this screening level assessment of fate and transport in the environment with additional, more certain data.

Finally, it is recommended that a protocol be developed that systematically describes the steps that should be followed when evaluating new energetic chemicals from an environmental liability standpoint. The protocol should start with a screening level evaluation as described here, but should also clearly identify additional steps for evaluation. The additional steps, which will likely be more resource intensive than a screening level assessment, should provide more detailed information about the chemicals of interest and their behavior in the environment. Also, the protocol should progress in a manner that removes uncertainty that is often found in screening level assessments and generate more conclusive information about a chemical's fate and toxicity.

APPENDIX A

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APPENDIX B

Summary Table of Estimated and Measured Chemical Parameters for Explosive Compounds

APPENDIX B. Measured and Estimated Physical and Chemical Properties of Explosive Comopounds Evaluated

Compound	Acronym	Molecular Weight (g)	Density (g/cm^3)	Melting Point (^{o}C)	K_{ow} (l/kg)	K_{oc} (L/kg)	K_d (ml/g)	Water Solubility (mg/L)	Henry's Law Constant (atm-m^3/mol)	VP solid (mm Hg)	Diffusion Coeff - Air cm^{2}sec	Diffusion Coeff - Water cm^{2}sec	Biodegradability Soil Aerobic	Anaerobic	Half-Life Soil (days)
Ammonium di(nitramido)amine	ADNA	135.04		**273.11**	**.72**	**3.359**		**115600**	**7.45E-09**	**2.30E-14**					**15**
Ammonium dinitramide	ADN	124.06		92	**.05**	**10.53**		**500000**	**1.27E-07**	**1.71E-12**					**15**
1,3,5,5-Tetranitrohexahydropyrimidine	DNNC	266.13		151-154	**0.072**	**1678**		**50100-73140**	**8.39E-15**	**5.27E-07**					**37.5**
Hexahydro-1,3,5-trinitro-1,3,5-triazine	RDX	222[R]	1.82[P,DC]	204-206[O]	8.7±0.28[Q]	2.00[DA]	1 to 3[F]	50[H]	1.96E-11[N,UC]	4.03E-09[R]	.0931[R]	8.87E-06	Negligible[J]	Significant Cometabolism[JA]	13140[G,QC]
		222.26[VA,RB,DC]	1.83[R]	205[VA,DC]	7.2[R]	2.13[CA]	0.2, 1.8, 6.4, 7.8[EA]	42[X,RB]	1.90E-11[R]	1.00E-09	0.074[N]	7.15E-06[N]			2.52E+06[ZA]
				204.1[RB,QC]	8.1[AA]	0.89, 1.87, 2.43[A]	0.8, 3.06, 4.15[EA]	42.3±0.6 @ 20°C[A]	1.2E-05[VA, NC]	4.1E-09[RB,AC]					0.17 to 0.25[AB]
				204.5[RC]	8.6[BA]	1.62, 2.10[J]	1.4, 4.2[A]	59.9±1.2 @ 25±0.2^{o}C[Z]	2.63E-11[AC]	1.0E-09[DC]					323 to 3900[OB]
					8.7[VA]	6.3E+01[VA]	1.6[J, FA,S]	59.9±0.6 @ 26.5^{o}C[A]	6.58E-12[DC]	1.95E-09[HC]					
					.86[NC,QC]	420[AC]	4.92 to 6.75[GA]	75.7±1.1 @ 30°C[H]	1.16E-11@ 20°C[H]	4.0E-9[NC]					
						.8 - 4.2[NC]	<1[HA]	60[VA]	2E-05[QC]						
							0.72TA	42.2[DC]							
							0.0-0.8[IA]	50@ 20°C[HC]							
							0.385, 0.049[FC]	38@ 20°C[NC]							
								42 @ 20°C[QC]							
								42.3 @ 20°C[SC]							
								40[LC]							
1,3,3,5,77-Hexanitro-1,5-diazacyclooctane	HCO	384.18		250	**0.0015**	**136700**		**153000-348100**	**1.53E-21**	**5.08E-11**					**240**
Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine	HMX	296[R]	1.90[N]	286[O,N,UC]	1.15[F,UC]	3.47[F,UC]	8.87-13.25[GA]	5[H,RB, LC]	3.50E-05[R]	3.00E-09[R]	0.78[R]	6.02E-06[N]	Negligible[E]	Accelerated[E]	14235[G, XA,QC]
		296.2[VA,JB]		276[O,VA]	3.9[R]	5.4[N, VA]	0.0-1.2[IA]	2.6[X]	2.60E-15[N, VA, NC, UC]	3.33E-13[N]	0.063[N]				1.17E+06[ZA]
		296.16[RB,QC]		276-280[RB,QC]	2.6[LA, VA]	2.83[E]	0 to 13.25[WA]	6.63[VA]	1.00E-04[KB]	2.6±0.01 @ 20°C[E]					
					0.6[BA]	6.310[LB]	<1 to 7.8[BC]	6.60[LB, NC]		5 @ 22-25°C[KA]					
					.13, .06[NC]	2.8[NC]		150[KC]		3.3E-16@20°C[RB]					
					.061[QC]			5 @ 25°C[SC]		3.3E-14[NC]					
					5.9[KB]			6.6@ 20°C[NC]		5.7±0.1 @ 30°C[E]					
								5@ 20°C[QC]							
Diammonium di(nitramido)dinitroethylene	ADNDNE	238.07		**127.89**	**.029**	**928.1**		**232800**	**5.27E-14**	**1.45E-06**					**37.5**
1,1-Diamino-2,2-dinitroethene	FOX-7	148.08		205	**.0014**	**30.6**		**1.00E+06**	**1.43E-12**	**1.04E-03**					**15.8**
Perchlorate		99.5[RB]					0.83[MB]	2.50E+05					None	Significant	

Note: Bolded entries are estimates based on EPI Suite

Compound	Acronym	Half-Life Water (days)	Photo-Sensitivity (Hours)	Hydrolysis (Years)	Hydroxyl Reaction Rate cm^{3}mole-sec	pKa	Water MCL (mg/L)	Water MMR PRG (mg/L)	Water SSL (mg/L)	Crystallography	Clean Up Standards Soils mg/Kg	Clean Up Standards Water ng/L	
Ammonium di(nitramido)amine	ADNA	15											
Ammonium dinitramide	ADN	135050											
1,3,5,5-Tetranitrohexahydropyrimidine	DNNC	37.5											
Hexahydro-1,3,5-trinitro-1,3,5-triazine	RDX	6.63^{ZA}	10.7^A	1.7^C			2^{IC,QC,VC}	6.11E-01	0.11		30^{PB}	2^{PB}	
		85045^{OB}	168^B				35^{XB}			Orthorhombic Crystals (from acetone)^O			
		7VB	120^E	Yes - Leaves, no Transforma-tion									
		3.21@250mV^{YB}	28.8 to 120^J										
		9E+06^{AC}	13.44^{ZB}										
1,3,3,5,77-Hexanitro-1,5-diazacyclooctane	HCO	60		.									
Octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine	HMX	0.46 to 0.5^{BB}	Signifcant^E	Not Significant^E	1.40E-13^T		400IC,QC,VC		0.4^{EC}				
		17.7^{ZA}	168^{EB}										
		1.4^{ZB}	4.56^{ZB}	Yes - Leaves, no Transforma-tion									
Diammonium di(nitramido)dinitroethylene	ADNDNE	37.5											
1,1-Diamino-2,2-dinitroethene	FOX-7	15.8											
Perchlorate								1.82	3.14			18$^{TA, SC}$	

Note: Bolded entries are estimates based or

References

A - Sikka et al. 1990
B - Spanggord et al. 1978
C - Hoff, Sommer, and Rosen 1973
D - Pennington et al. 1995
E - Spanggord et al. 1982
F - McGrath 1995
G - Phelan and Webb 1998
H - Flemming et al. 1996
I - Townsent et al. 1996
J - Spanggord 1980
K - Bradley et al. 1994
L - Jenkins et al. 2000
M - HDSB 1996
N - Rosenblatt et al. 1989
O - Meyer 1977
P - Kaye 1980
Q - Banerjee et al. 1985
R - IRP 1994
S - Spalding and Fulton 1988
T - Howard and Merylan 1997
U - Estimated According to Lyman et al. 1982
V - Ro et al. 1996
W - Burrrow et al. 1989
X - McGrath 1996
Y - Haderiein et al. 1996
Z - Banerjee, Yalkowsky, and Valvani 1980
AA - Major 1984
BA - Jenkins 1989
CA - Tucker et al. 1985
DA - Rosenblatt 1986
EA Hale, Stanford, and Taft
FA - Tsai et al. 1985
GA - Leggett 1985
HA - Ainsworth et al. 1993
IA - Myers et al (In Preparation)
JA - McCormick et al. 1981
KA - Glover and Hoffsommer
LA - Major 1989
MA - Deam 1985
NA - Urbanski 1964
OA - Verschueren 1983
PA - Merck 1983
QA - Haynes and Smith 1981
RA - Leggett, Jenkins and Murrman 1977
SA - Pennington and Patrick 1990
TA - Selim and Iskandar 1994
UA - Howard et al. 1991
VA - ATSDR
WA - Townsend and Myers 1996
XA - Rodacy and Leslie 1995
YA - Herman and Frankenberger 1998
ZA - Deliman and Gerald 1998

AB - Price et al. 1998
BB - McCormick et al. 1984
CB - Biyares and Jenkins 200
DB - Pennington et al. 1999
EB - Bedford et al. 1996
FB - Kayser et al. 1984
GB - Demo 1 Report
HB - TNRCC, 2002
IB - RAIS, 2002
JB - CHEMFATE, 2002
KB - EAP SSL Table
LB - Talmage et al. 1999
MB - Susarla et al. 1999
NB - USEPA 1986
OB - Pennington et al. 2001
PB - Black and Veatch 1995
QB - Ravikrishna et al. 2002
RB - Hewitt 2002
SB - Best et al. 1998
TB - Walsh and Jenkins 1992
UB - Walsh 1990
VB - Cataldo 1990
WB - Shepodd et al. 1997
XB - United States Army Environmental Hygiene Agency
      Aberdeen Proving Ground, 1985
YB - Price et al. 1998
ZB - Spanggord et al. 1983
AC - Spanggord et al. 1980
BC - Townsend and Adrian 1996
CC - Henderlein et al. 1996
DC - Ainsworth et al. 1993
EC - Thiboutot et al. 200
FC - Speitel and Yamamoto 2002
GC - Etnier 1987
HC - Phelan and Webb 1997
IC - Lynch, Brannon and Joseph 2002
JC - Collette et al. 1999
KC - Major 1999
LC - Hawari 2000
MC - Basunia and Landsberger 2001
NC - Groom et al. 2002
OC - Sung et al. 2002
PC - Aken and Schnoor 2002
QC - Tomkins 200
RC - Farber and Srivastava 1979
SC - Gorontzy et al. 1994
TC - Jenkins, Legget, and Ranney 1999
UC - McGrath 1995
VC - Thiboutot, Ampleman, and Hewitt 2002
WC - Webb et al. 1999
XC - Weast and Astle 1980

8.2   TOXICITY FINAL REPORT FROM AMEC (CLICK BELOW)

Toxicological Screening of Perchlorate Replacements Using the Commercial
Bio-Rad "ADME/Tox" Model

Draft Report

Conducted in Support of the
Strategic Environmental Research & Development Program

"Synthesis, Evaluation, and Formulation Studies on New Oxidizers
as Alternatives to Ammonium Perchlorate in DoD Missile Propulsion
Applications."

Submitted to:

Naval Surface Warfare Center
Indian Head, MD

Submitted by:

AMEC Earth & Environmental
Boston, Massachusetts

June 30, 2006

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1.0   INTRODUCTION

The military is continuously researching and developing improved replacement propellants and explosive materials for use in munitions. Chemical propellants and explosives can undergo research and development for years. During these periods, they are tested for a variety of chemical and physical properties related to their suitability for use in munitions. Moreover, at any one time there can be numerous chemicals in various stages of development. Significant number of personnel as well as large financial resources are dedicated to the development of these chemicals. Identification of less suitable chemicals or ones that carry additional environmental liability early in the development process aids in focusing resources on those chemicals with maximum application potential and minimal environmental liability.

Historically, the evaluation of success or failure of these chemicals has focused on their performance as propellants and/or explosives, whereas little attention has been paid to the potential environmental liability. More recently, environmental mobility, persistence and potential toxicity issues related to perchlorate have highlighted the importance of trying to anticipate the environmental risk before beginning large-scale production of a new oxidizer. In other words, assessment of the environmental impact needs to be performed before embarking on an expensive synthesis effort.

Recognizing this, the Naval Surface Warfare Center (NSWC) contracted with AMEC Earth and Environmental (AMEC) to estimate the fate-and-transport and toxicological properties of new oxidizers proposed to replace perchlorate in rocket propellant formulations. AMEC's predictive assessment uses a uniquely defined architecture to evaluate whether the new oxidizers proposed to replace perchlorate are more or less environmentally benign relative to perchlorate.

Four energetic chemicals are proposed for perchlorate free tactical missile formulations under the Strategic Environmental Research and Development PP-1403 Synthesis, Evaluation, and Formulation Studies on New Oxidizers as Alternatives to Ammonium Perchlorate in DoD Missile Propulsion Applications. These include the inorganic oxidizer ammonium di(nitramido)amine (ADNA) whose chemical structure is presented in Figure 1; the cyclic nitramine/gem-dinitro compound 1,3,5,5-tetranitrohexahydropyrimidine (DNNC) whose chemical structure is presented in Figure 2; and 1,3,3,5,7,7-hexanitro-1,5-diazacyclooctane (HCO) whose chemical structure is presented in Figure 3; and diammonium di(nitramido) dinitroethylene (ADNDNE) whose chemical structure is presented in Figure 4[1].

A previous report conducted by AMEC (AMEC, 2004) used the USEPA EpiSuite model to estimate selected fate, transport, and toxicological information on the four subject chemicals and discussed the findings relative to the fate, transport, and toxicity with respect to ammonium perchlorate. It also paired the above compounds with "surrogate" compounds (analogous in structure) so that a relative frame of reference could be developed as the compounds were processed through the EpiSuite model. One important reason for this is that ADNA and ADNDNE are both polar structures. Most QSAR routines that evaluate fate-and-transport are not programmed to process polar

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[1] The EPI Suite model is unable to evaluate ionic bonds such as those found in ADNA. AMEC used a surrogate for ADNA, which can be viewed in Figure 5.

structures. The reason for is most likely due to the fact that highly water soluble compounds are, in most cases, easily excreted by animals and therefore don't present a problem from the perspective of "persistent, bioaccumulative, or toxic" compounds (PBTs).
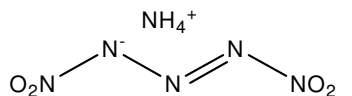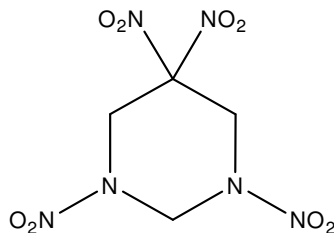
ρ = 1.76 g/mL (calc)
ΔHf = +43 kcal/mole (calc)

Figure 1. ADNA

ρ = 1.82 g/mL
ΔHf = +11 kcal/mole
mp = 151-4 degrees C

Figure 2. DNNC
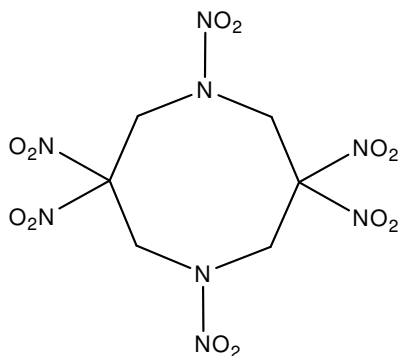
ρ = 1.875 g/mL
ΔHf = -6.52 kcal/mole
mp = 250 degrees C (dec)

Figure 3. HCO
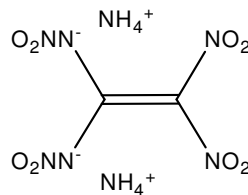
ρ = 1.77 g/mL (calc)
ΔHf = 4.02 kcal/mole (calc)

Figure 4. ADNDNE

2.0   PURPOSE

The purpose of this research was to continue to identify methods or strategies by which munitions replacement compounds could be "screened" for environmental liability. Because most of these replacement compounds are currently within the R&D phase of development, the screening techniques that would be considered the most useful would be predictive computer models that provide important hazard characteristics (e.g. toxicity) <u>before</u> they are manufactured, distributed and released to the general environment. The only way to effectively predict hazard from an "unknown" chemical is through the use of highly sophisticated computer models that are based on two or more quantitative structure-activity relationships (QSAR) sets of data.

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Following the evaluation of fate-and-transport of the above compounds using EPI Suite, the next logical step was to evaluate QSAR models that may be able to predict mammalian toxicity, metabolism and/or environmental degradation. A careful web-based search identified the Bio-Rad "ADME/Tox" Know-It-All model, from the perspective of cost/benefit, as the most effective QSAR routine on the market. Once this model could be learned and run effectively, it would be able to achieve the goal of estimating toxicity, degradation and metabolism of the above perchlorate replacement compounds.

3.0 METHODS

The essential purpose of a QSAR model is to predict, with a reasonable amount of accuracy and a minimum degree of uncertainty, a physical, chemical or biological property of a new or unknown chemical based on the relationship (usually linear) of the colligative properties of a host of other compounds from a similar chemical class. QSAR "models" can vary from a simple linear regression relationship between two variables (allowing interpolation between data points) to extremely complex multiparameter, multifactorial functions. In toxicology, the most commonly parameter that is used to predict or "regress" toxicity is Log P, which is the logarithm of the octanol-water partition coefficient. The Log P is, in turn, inversely related to the water solubility of the compound. Generally speaking, the greater the water solubility of a compound, the less toxic it will be to humans or wildlife is assumed.

Predictive QSAR software can use many other types of prediction techniques or mechanisms, which may include correlation of a physical, chemical or biological endpoint with any of the following: presence/type of functional groups, molecular connectivity, molecular surface area, "fragments", Log P, molecular weight, boiling point, melting point, vapor pressure, Henry's Law Constant. Once the model is built using a "training set", it is then validated by applying other chemicals with "known" colligative properties (usually left out of the training set on purpose) and seeing how accurate/precise the predicted value is against its "known" value. An in depth explanation of how each QSAR subroutine runs is not possible for this report, but, if the reader requires more details, Bio-Rad has supplied references (Appendix A).

A demonstration version of the Bio-Rad ADME/Tox QSAR model showed that the above four compounds, according to scientific support staff at Bio-Rad, "fell within the chemical space of the toxicity and metabolism libraries" that were stored within the model. This means that the property of the chemical of interest (e.g., ADN) fell in between the highest and lowest value for whatever parameter of interest was being measured, thus allowing "interpolation" along the regression line and, consequently, a predicted range or value as a result.

The ADME/Tox "Know-It-All" model was then ordered from Bio-Rad (New Jersey), with the following subroutines chosen as endpoints to further evaluate the potential hazard of perchlorate replacement compounds:

- Bioaccumulation – the potential for a chemical to accumulate within an organism
- Bioavailability – the degree to which a chemical partitions into an organism
- First-Pass Metabolism – how a chemical is transformed before cycling through the gastrointestinal system (i.e. no reabsorbtion from processed bile)

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- Immunotoxicity – the toxicity of a chemical to any component of the immune system
- Irritation – the potential for a chemical to induce skin irritation (redness, swelling, edema)
- Metabolism – how a chemical is transformed by an organism (includes photodegradation)
- Mutagenicity – the potential for a chemical to cause a cell to mutate (e.g. Ames test)
- Neurotoxicity – the potential for a chemical to alter or damage nerves and/or impulse transmission
- Oncogenicity – the potential for a chemical to induce cancer (chronic effect)
- Sensitivity – the ability of a chemical to sensitize an individual (e.g. allergic reactions)
- Teratogenicity – the potential for a chemical to induce birth defects

Dr. Michael Gray (AMEC Portland) and Dr. Stephen Clough (AMEC Westford) then employed both the on-line tutorial program, as well as the CD-based tutorial program, to learn how to input data, run the program, and output results from the program. The first step is inputting data using the "DrawIt" subroutine, as illustrated (using HMX) below:
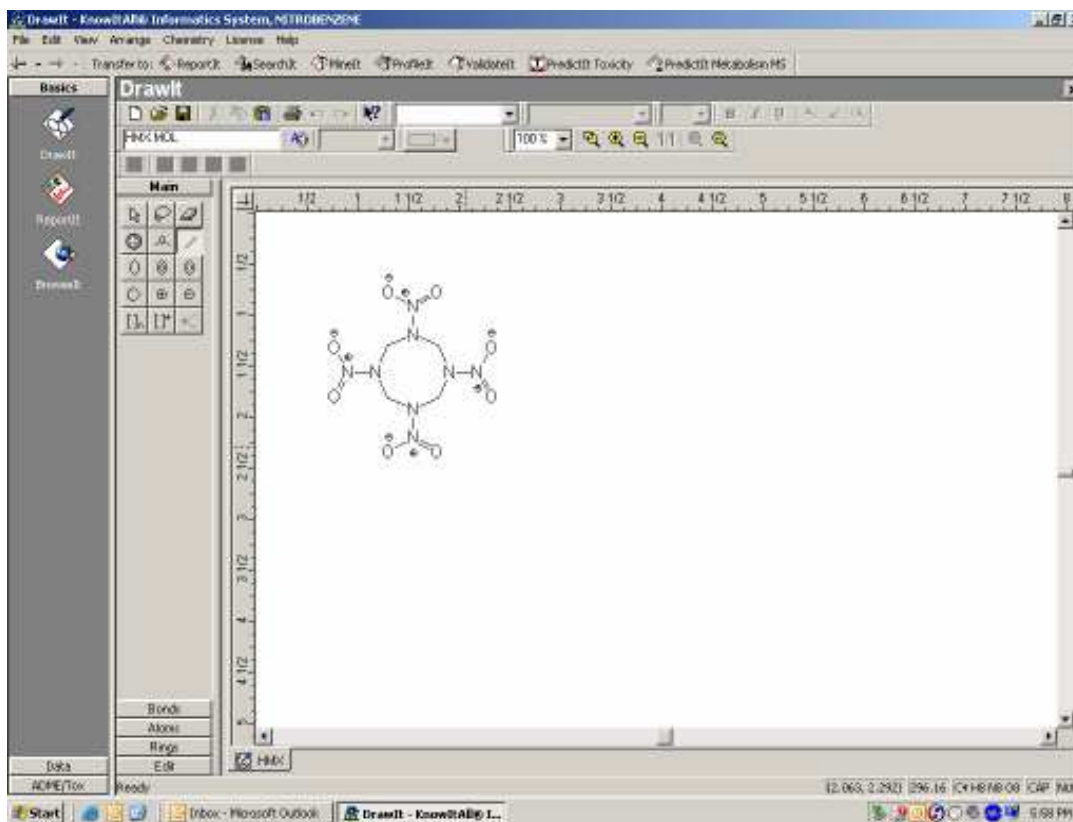
Following the entry of the structure into "DrawIt", the whole molecule is then "selected" using a lasso icon and the "Check Chemistry" function is the chosen from the main "Chemistry" drop-down menu at the top of the screen. Once the structure of the compound is drawn, it can be saved as a "mol" file (pronounced "mole file").

The next step is to make sure all of the available databases needed for each individual ADME/Tox subroutine are downloaded from the software memory. This is done by selecting the "SearchIt" icon at the top of the screen and then importing all of the "Licensed Databases" into the program:
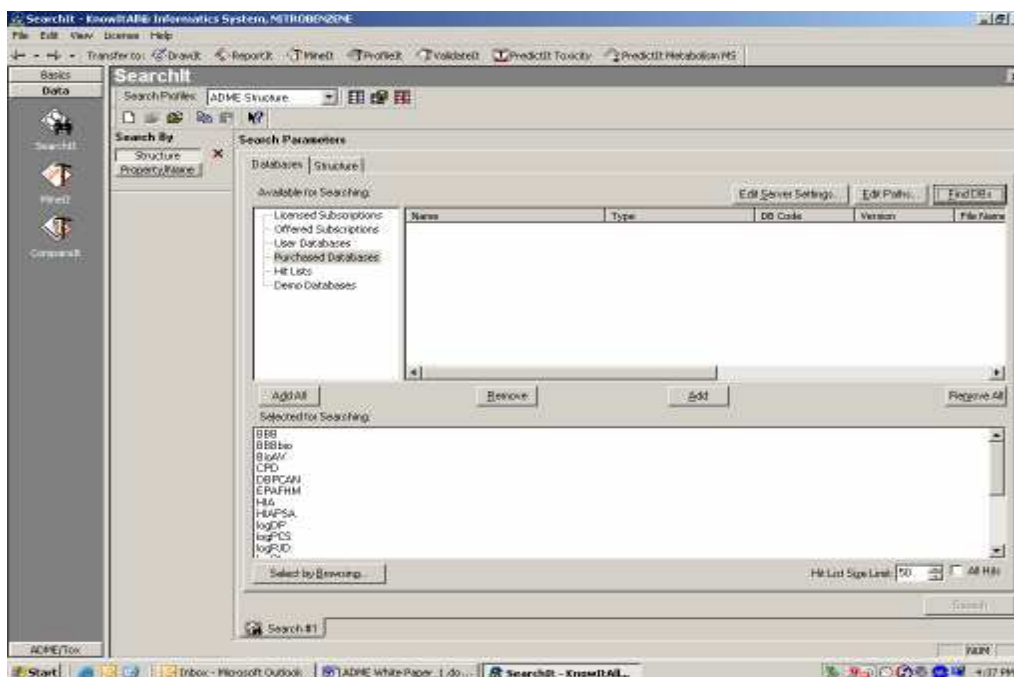
Once this is done, the user reselects the "DrawIt" window and then chooses "ProfileIt" to generate the toxicity values generated by each individual QSAR routine:
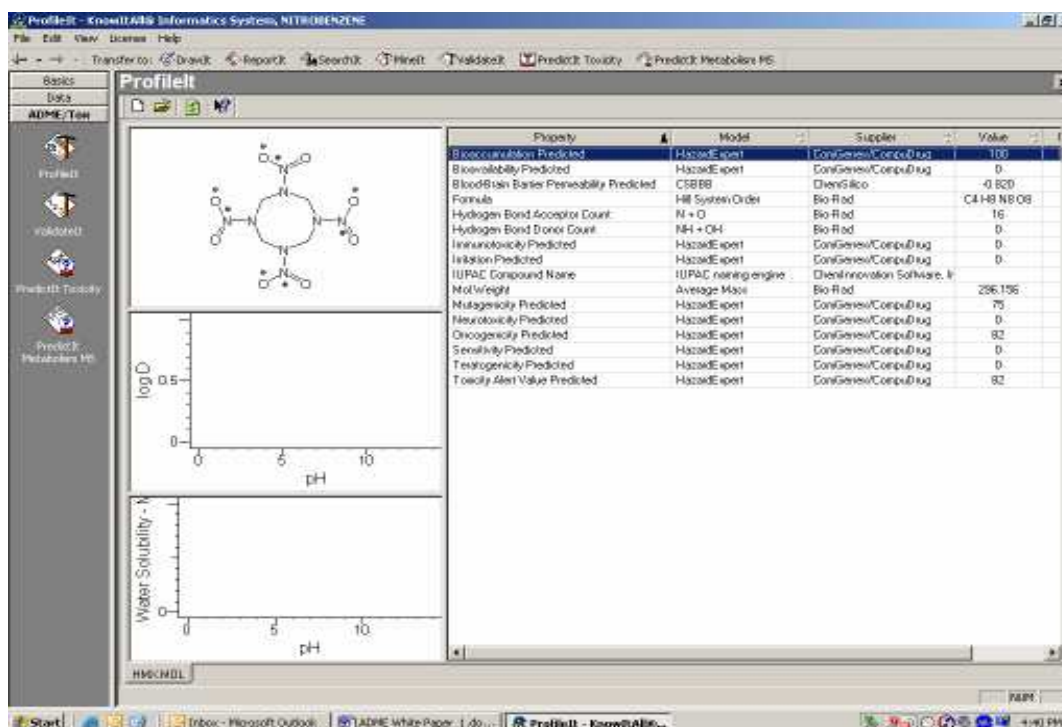
The data generated from "ProfileIt" generally contains the same subset of data that "PredictIt Toxicity" contains, so there is usually no need to run the latter routine.

The final step in the Bio-Rad ADME model is the "PredictIt Metabolism" subroutine. This program is probably the most sophisticated and complex of the ADME/Tox suite of subroutines. It has the ability to identify just about every metabolite that can possibly be envisioned (and also metabolites of metabolites) for any particular compound, but it also has the drawback of being an "all or none" function in that, it appears, some types of molecules just will not run at all. The following output is for Fox 7:
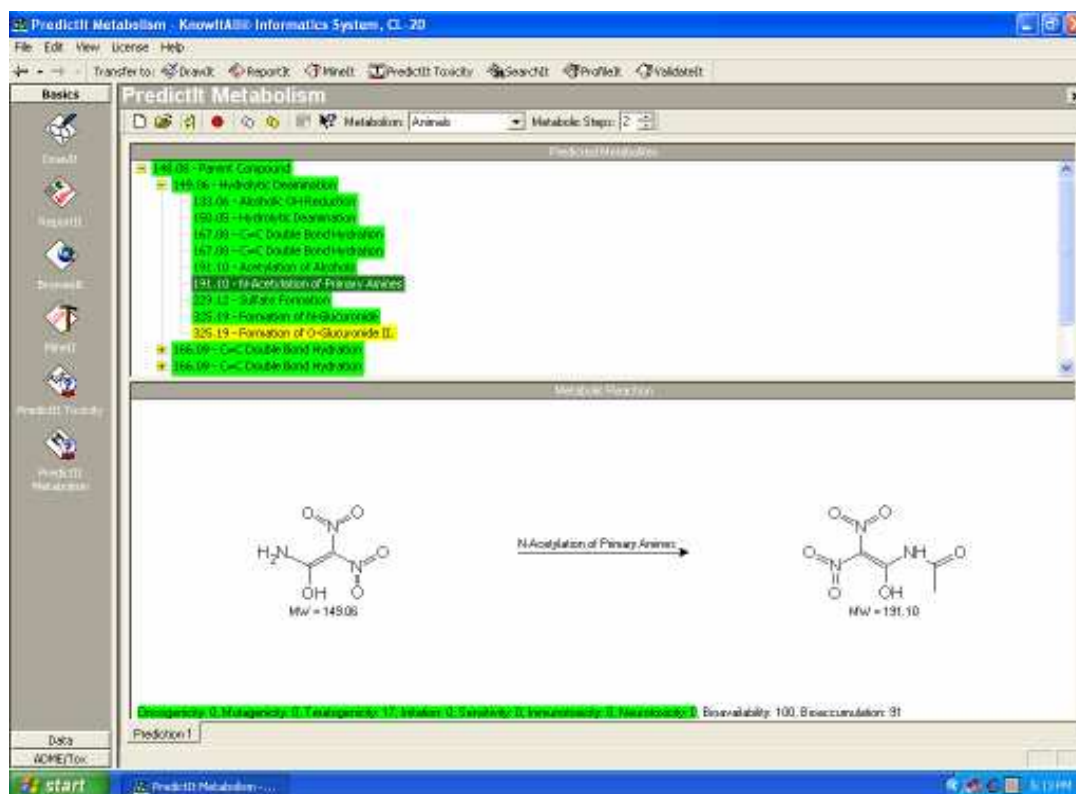
The output of any subroutine of the model can generally be copied into either Microsoft Word or Excel. This is advised because the generic output is usually difficult to manipulate within each individual window. As was done with EPI Suite, the perchlorate replacement compounds (Fig. 1) were paired with the following compounds:
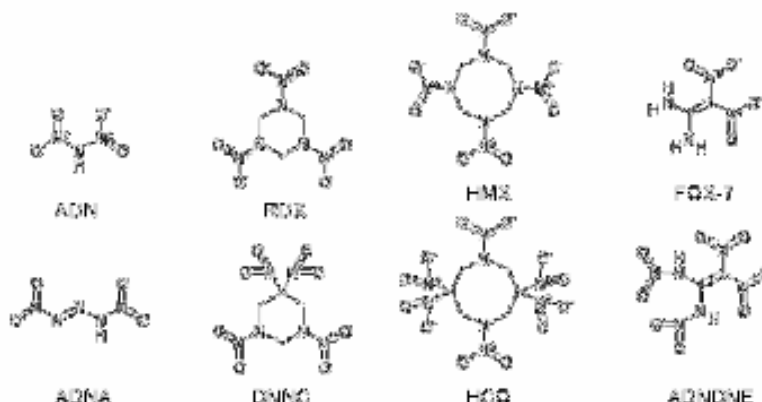
ADN was paired the ADNA; DNNC was paired with RDX; HCO was paired with HMX; and ADNDNE was paired with FOX-7.

4.0   RESULTS

Table 1 presents the Predicted Toxicity Report Summary for all of the compounds simulated on the ADME/Tox software. The only "Alerts" generated were for "Oncogenicity" (potential to induce cancer) and "Mutagenicity" (potential to cause a mutation) for the both the DNNC/RDX and HCO/HMX pairs. This result indicates that the choice of the surrogate analog compounds for both DNNC and HCO were most likely correct as the model responded to them in the exact same way. The simulation of the remaining compounds resulted in an output of "zero". Bioaccumulation scores ranged from 66 (FOX-7) to 100 HCO/HMX, meaning that most of the compounds tested by the computer program had a moderate to very strong propensity to bioaccumulate in an organism.

Table 2 presents the Predicted Metabolism Report Summary for all of the compounds simulated with the metabolism subroutine. All of the more detailed metabolism output, i.e. the graphical output that presents the structure of the parent compound and its respective metabolite, are presented in Appendix B. Because metabolic reactions can often lead to the formation of multiple metabolites (generated from a single parent compound), some of the simulation runs were run with more than one "Metabolic Steps". Therefore, some of the output may seem redundant because the computer program was set to process more than two steps. For example, if compound was hydrolyzed, it is possible that the reactive product may then be conjugated to an endogenous compound, such as a glucuronide.

None of the substances were accepted by the Plant Metabolism subroutine. Therefore, all output was in the form of "No Results".

With regard to Animal Metabolism, most of the output was negative. ADNDNE and FOX-7 were the only two compounds that the ADME/Tox program was able to simulate with regard to animal metabolism. The graphical output for these structures is presented in Appendix B. ADNDNE can be metabolized via the following metabolic pathways:

- Double bond hydration
- Alcoholic OH reduction
- Formation of glucuronide (conjugated to carbohydrate)
- C=C Double bond oxidation
- Conjugate hydrolysis

Some of these ADNDNE metabolites showed some positive results in terms of toxicity. For example, the alcoholic OH reduction of the glucuronide conjugate resulted in a 53 rating (out of 100 possible on a probability scale) for "Teratogenicity". The vast majority of the metabolites, however, showed little (<30) to no (0) potential for toxicity.

The ADME/Tox program was also able to process FOX-7 via the following metabolic pathways:

- Double bond hydration
- Alcoholic OH reduction
- Formation of O-glucuronide (conjugated to carbohydrate)
- Formation of N-glucuronide (conjugated to carbohydrate)
- C=C Double bond oxidation
- N-acetylation of primary amine
- Conjugate hydrolysis
- Secondary amine dealkylation
- Secondary amine hydroxylation

As seen with ADNDNE, a few of the FOX-7 metabolites showed some slight potential for toxicity, but none ranked higher than a score of 53 (for "Teratogenicity").

FOX-7 was the only compound to be metabolized via a "first pass" mechanism (generally interpreted as the metabolism of a compound the "first time through" the liver, i.e. there is no secondary metabolism due to reabsorption of bile). This "first pass" subroutine was described by the Bio-Rad vendor as of lessor importance than the animal metabolism subroutine, so it is not of significance to this research.

With regard to photodegradation, only DNNC/RDX and HCO/HMX were actively processed by the ADME/Tox computer program. The structural results for this reaction are also presented in Appendix B. The photodegradative by-product for all four of these compounds was principally a rearrangement of the nitro- group constituents around the ring structure, followed by a reduction of one or more of the nitro- groups. This structural change caused by the modeled photodegradation process did not appear to result in any change in the status of the toxicity of the metabolite (relative to the parent compound).

5.0   DISCUSSION

None of the parent compounds that were processed for toxic endpoints using the ADME/Tox model showed any "response" for teratogenicity, irritation, sensitivity, immunotoxicity, neurotoxicity or bioavailability. Although much of this "negative data" appears suspicious, a call to the Bio-Rad technical representative assured us that a "zero result" does not mean that the chemical was not processed by the respective subroutine. To the contrary, it means that the chemical has a very low potential to cause toxicity for that particular toxic effect category. From the standpoint of perchlorate replacements, this is good news in that the screening process for the replacement compound showed no "positive" result.

One concern may be the fact that DNNC, RDX, HCO and HMX showed some potential for oncogenicity and mutagenicity. That result, however, appears to be based on the presence of a nitroso- group within the ring structure. Since the carcinogenic activity of nitrosamine compounds is principally a function of primary amine groups, it is unlikely that the secondary or tertiary nitroso- groups within these energetic munitions compounds would be able to show carcinogenic activity. It is already known that RDX will not cause mutations in laboratory tests, but it does have the potential to cause cancer in laboratory animals (although the evidence is not strong). There is also no evidence that exists to show RDX causes cancer in humans.

DNNC, RDX, HCO and HMX all showed the potential, according to the ADME/Tox output, to undergo photodegradation. It is interesting, from this viewpoint, that ADNA, ADN and ADNDE did not respond to the photodegradation model because EPI Suite showed that most of these munitions compounds had the potential to photodegrade.

This research has shown that the ADME/Tox software has many different powerful evaluative tools available to assess the physical, chemical and biological parameters for a host of different organic compounds. Unfortunately, the fact that 56 out of a total of 64 toxicity endpoints (8 compounds x 8 endpoints) ended up with a result of "zero" leaves the user with a strong impression that the model is not "sensitive" when it comes to discerning adverse effects. This may simply be a result of the content of the "training set" used to construct the QSAR subroutines within the model. For example, if there are very few compounds that contain two or more nitrogens, the "confidence" of the model may not be high and therefore the decision process may instruct the model to use a "zero" for the result (even though the compound being modeled may fall within the "chemical space" of the QSAR training set).

Another drawback of the model is that is lacks transparency. The best way to view a particular result is to see it as a single data point within the library of compounds that it is being tested against. For example, if "Irritation" is plotted against Log P for the complete training set, then one of the compounds tested could be highlighted within that plot to show where it falls on the graph within the training set population. In fact, there is still no way to tell whether a result of "zero" has any real meaning to the user, because there is only one value reported for each individual compound.

Based on this research, one can conclude that:

- With regard to the Predictive Toxicity model, only 8 of the 64 toxicity endpoints resulted in ADME/Tox model output that indicated a high probability of an adverse effect. This is a good result in terms of whether the replacement compounds may pose a hazard to humans or wildlife. The high probability endpoints were "Oncogenicity" and "Mutagenicity" for DNNC, RDX, HCO and HMX. All of the output for the remaining endpoints (teratogenicity, irritation, sensitivity, immunotoxicity, neurotoxicity and bioavailability reported negative results (zero).

- With regard to the Predictive Metabolism model, no results were reported in the output for Plant metabolism. ADNA and ADN were not accepted ("No Result") for any of the Predictive Metabolism subroutines. DNNC, RDX, HCO and HMX were "predicted" to be vulnerable to photodegradation. ADNDNE and FOX-7 were the only two compounds that the model was able to process with regard to simulating animal metabolism.

- For compounds that did show a "positive" result with regard to metabolism or photodegradation, the model output is instructive in showing a long list of potential metabolites that are possible and, in some cases, secondary metabolites.

- The model itself, though a very sophisticated tool, is not intuitive in terms of learning or documentation. The authors believe that the best way to learn this model would be a tutorial with a person who knows how to run the model well. The model also lacks transparency in terms of defining what the some of the output means. For example, it would be helpful to see where the value in question may lie in relation to the training set used to develop the QSAR (i.e. as a Cartesian graph). Additionally, an output value of "zero" does not indicate that the chemical property or parameter in question falls outside of the limits of the training set used to develop that particular QSAR algorithm. This was discussed with the model developers, who acknowledged that a result of zero may give the operator a false impression that the input was "rejected" or did not carry sufficient information to process the input value.

- Additionally, there is little to no "metadata" available within the software to tell the user exactly what the results mean. For example, some output values had no units associated with them.

- Finally, initial runs determined that the quickest way to present the output was to copy it from the program's output window into a work processing file or a spreadsheet. This can be cumbersome process. Later discussions with the technical staff identified a faster way to quickly transfer the proprietary model output into an Excel spreadsheet.

6.0   REFERENCES

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TABLES

PredictIt Toxicity and Metabolism Output

Table 1

Predicted Toxicity Report Summary
Hazard Screening of Perchlorate Replacements

Compound	ADNA		ADN		ADNDNE		FOX7		DNNC		RDX		HCO		HMX	
Hazard	P	Alert	P	Alert	P	Alert	P	Alert	P	Alert	P	Alert	P	Alert	P	Alert
Oncogenicity	0		0		0		0		82		82		82		82	
Mutagenicity	0		0		0		0		75		75		75		75	
Teratogenicity	0		0		0		0		0		0		0		0	
Irritation	0		0		0		0		0		0		0		0	
Sensitivity	0		0		0		0		0		0		0		0	
Immunotoxicity	0		0		0		0		0		0		0		0	
Neurotoxicity	0		0		0		0		0		0		0		0	
Bioavailability	0		0		0		0		0		0		0		0	
Bioaccumulation	91		91		91		66		91		91		100		100	
P	Probability Rating															
Alert Message	Highly Probable			Not Probable												

Table 2

**Predicted Metabolism Report Summary
Hazard Screening for Perchlorate Replacement Compounds**

Compound	ADNA	ADN	ADNDNE	FOX7	DNNC	RDX	HCO	HMX
Metabolism								
Plant	NR	NR	NR	NR	NR	NR	NR	NR
Photodegradation	NR	NR	NR	NR	P	P	P	P
First Pass	NR	NR	NR	P	NR	NR	NR	NR
Animal	NR	NR	P	P	NR	NR	NR	NR
Predicted	P							
No Results	NR							
Specific Results are attached								

ATTACHMENT A

References for Bio-Rad Model Development

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PredictIt Log P

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ATTACHMENT B

Predicted Metabolism Output from the Bio-Rad ADME/Tox Model

Predicted Metabolism Reports for Perchlorate Replacement Compounds

ADNA
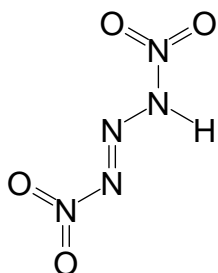
No Results for plants, photodegradation, first pass, or animal metabolism.

ADN
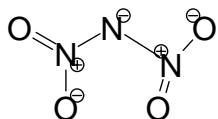
No Results for plants, photodegradation, first pass, or animal metabolism.

ADNDNE

No Results for photodegradation, plants, or first pass.

Animals   Two Metabolic Steps

Report I

C=C Double Bond Hydration

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91

Alcoholic OH Reduction

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 70, Bioaccumulation: 91

Formation of O-Glucuronide II.

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0,   Bioavailability: 30, Bioaccumulation: 66
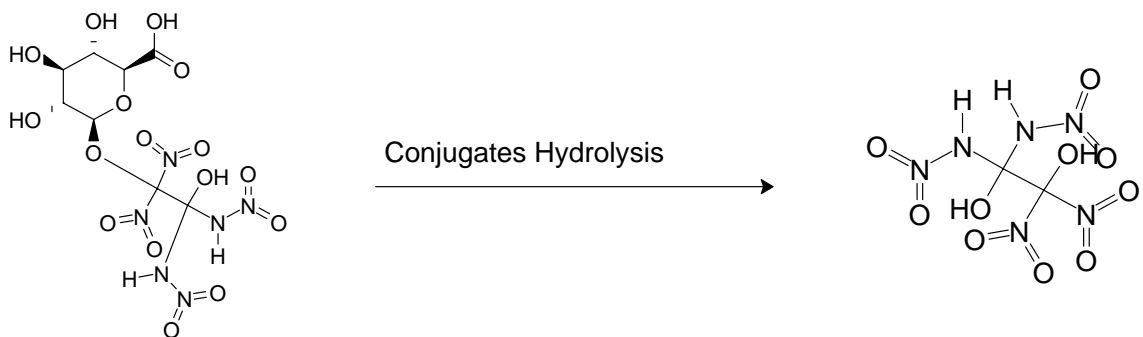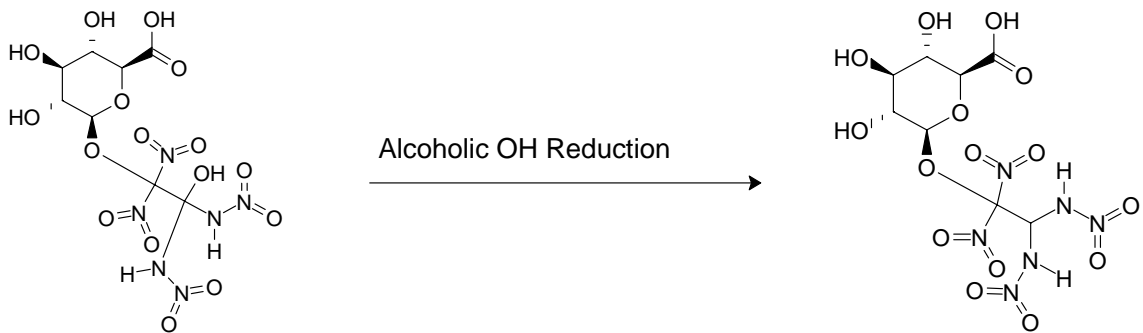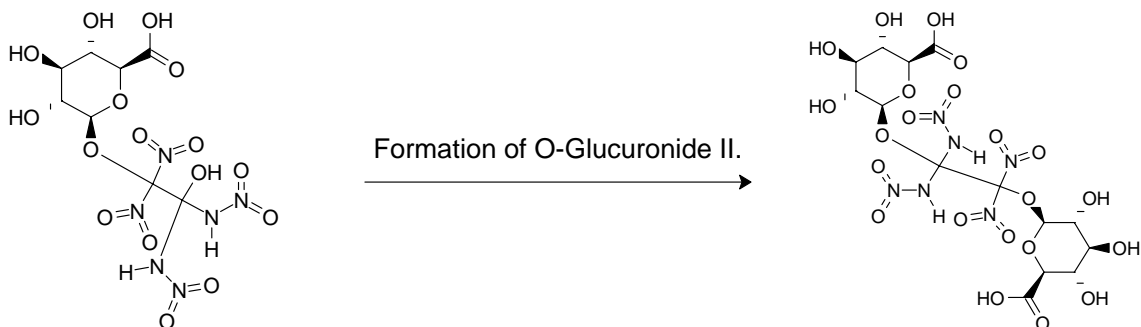
Report II

C=C Double Bond Hydration

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91

Alcoholic OH Reduction

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 70, Bioaccumulation: 91
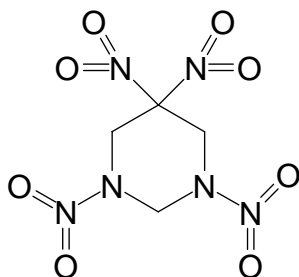
Formation of O-Glucuronide II.

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0,   Bioavailability: 30, Bioaccumulation: 66
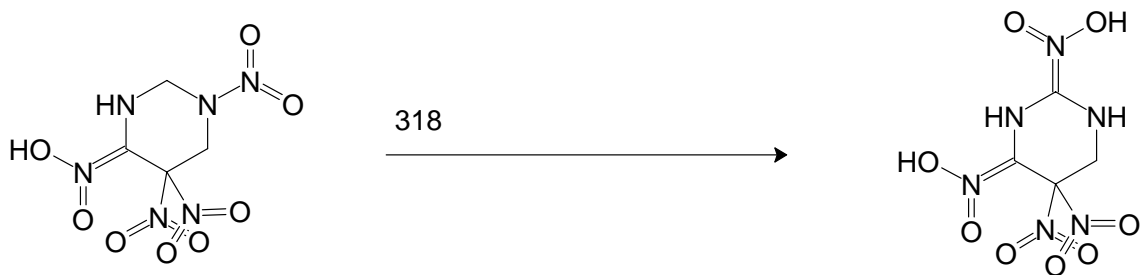
Report III

C=C Double Bond Oxidation

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91

Alcoholic OH Reduction

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91

Alcoholic OH Reduction
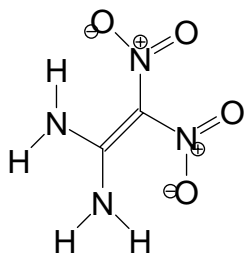
Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91

Formation of O-Glucuronide II.

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0, Bioavailability: 0, Bioaccumulation: 66

Formation of O-Glucuronide II.

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0, Bioavailability: 0, Bioaccumulation: 66

ADNDNE

Animals   Nine Metabolic Steps

Report I

C=C Double Bond Hydration

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0, Bioavailability: 0, Bioaccumulation: 91

Alcoholic OH Reduction

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 70, Bioaccumulation: 91
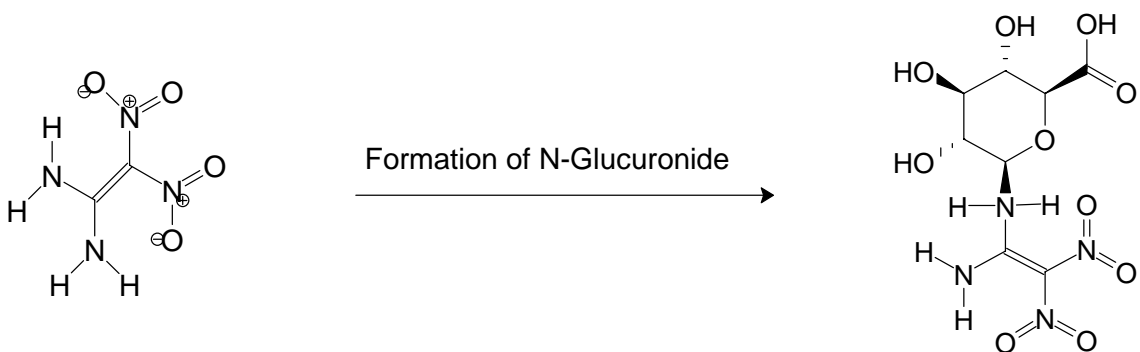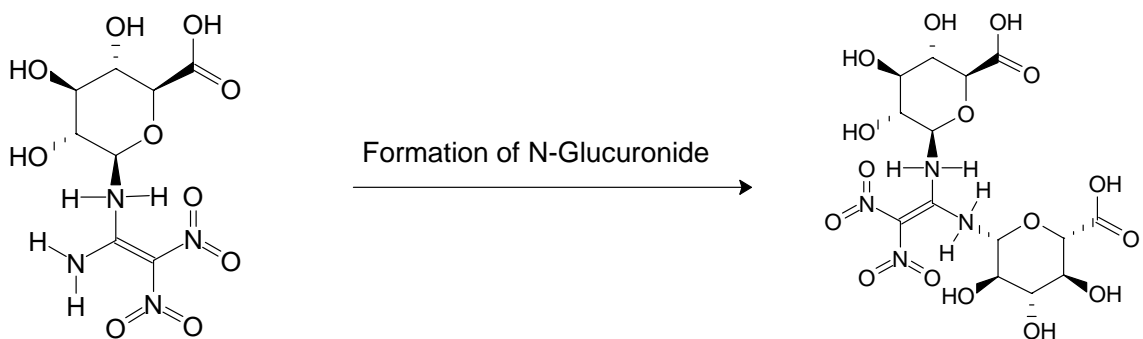

Formation of O-Glucuronide II.

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0,   Bioavailability: 30, Bioaccumulation: 66
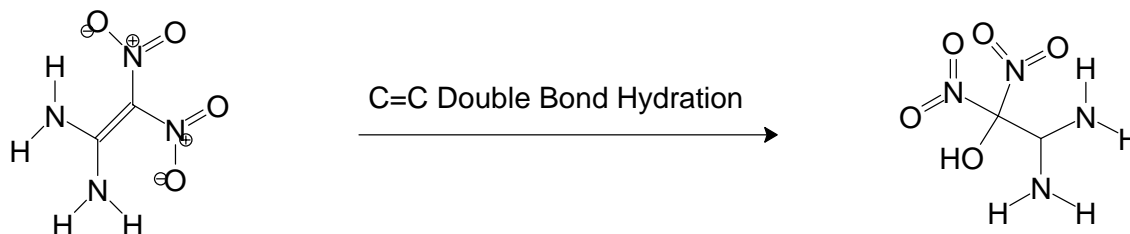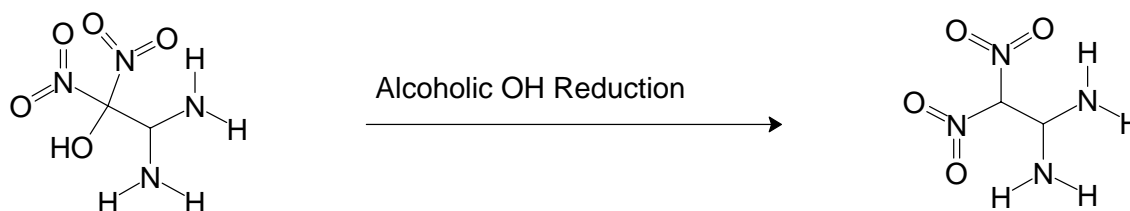

Conjugates Hydrolysis

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60

Conjugates Hydrolysis
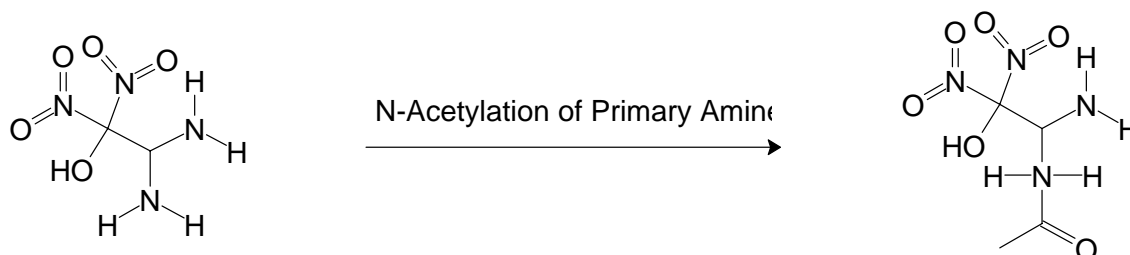
Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91

Report II

C=C Double Bond Hydration

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91

Alcoholic OH Reduction
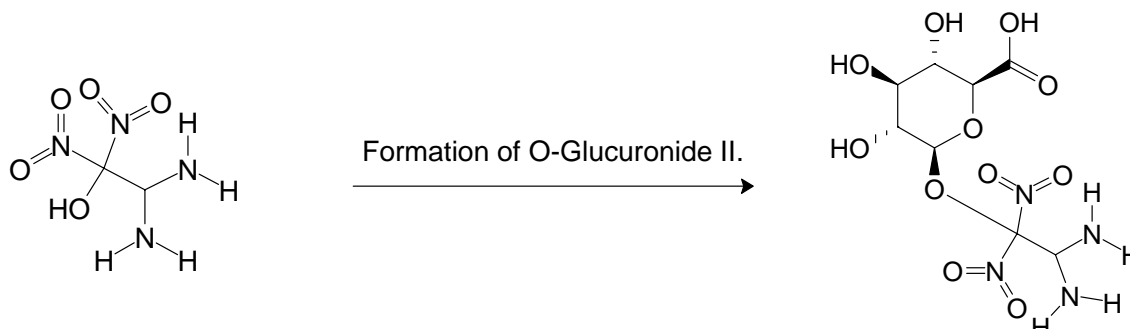
Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 70, Bioaccumulation: 91

Formation of O-Glucuronide II.

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0,   Bioavailability: 30, Bioaccumulation: 66
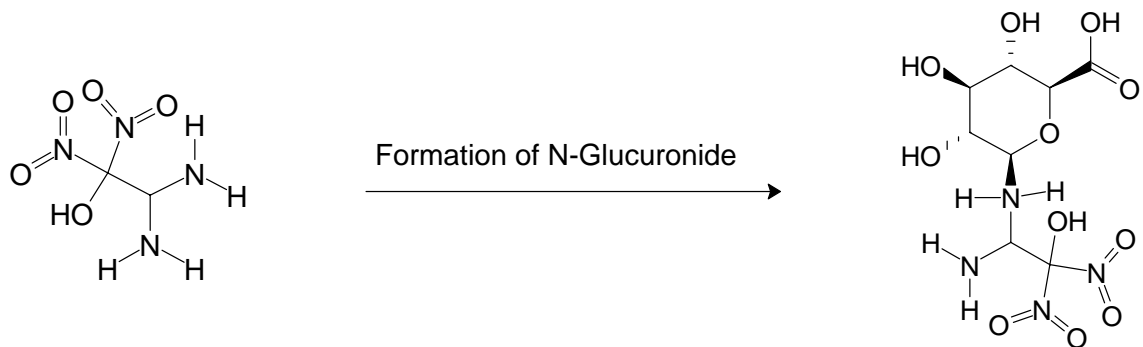

Conjugates Hydrolysis

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60

Conjugates Hydrolysis

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91

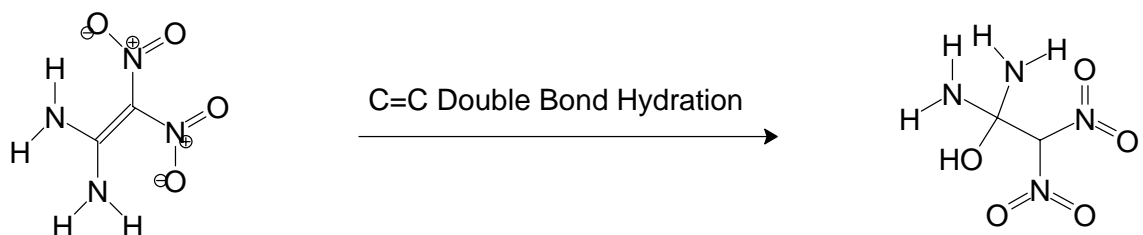## Report III

C=C Double Bond Hydration

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91

Alcoholic OH Reduction
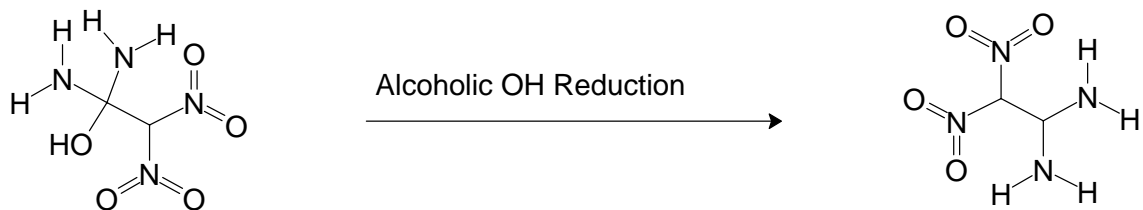
Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91

Alcoholic OH Reduction

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91
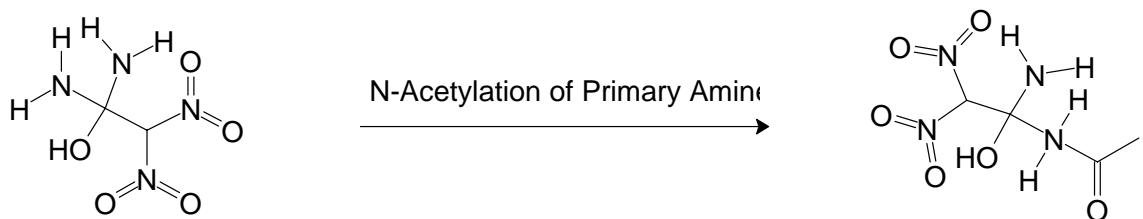
Formation of O-Glucuronide II.

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0,   Bioavailability: 0, Bioaccumulation: 66
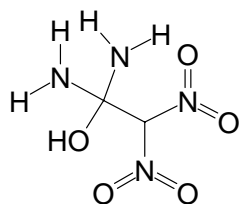

Conjugates Hydrolysis

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60
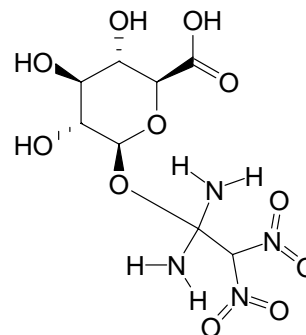

Alcoholic OH Reduction

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60
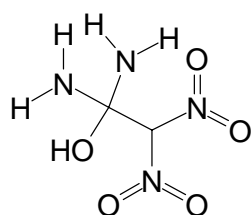

Conjugates Hydrolysis

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity:
29, Neurotoxicity: 0,   Bioavailability: 30, Bioaccumulation: 66

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity:
29, Neurotoxicity: 0,   Bioavailability: 30, Bioaccumulation: 60

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0,
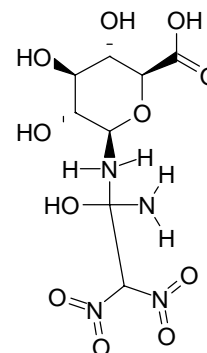Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0,
Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0, Bioavailability: 0, Bioaccumulation: 66
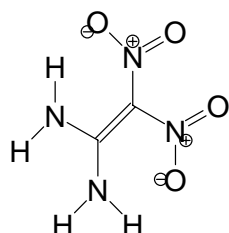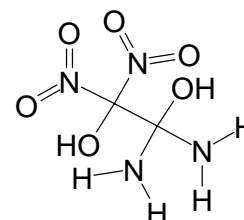

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0, Bioavailability: 0, Bioaccumulation: 66
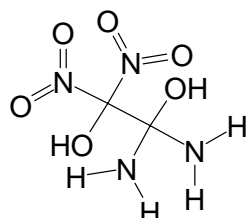

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0, Bioavailability: 0, Bioaccumulation: 66

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91
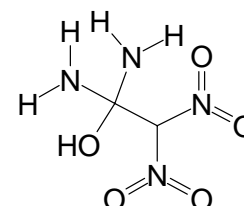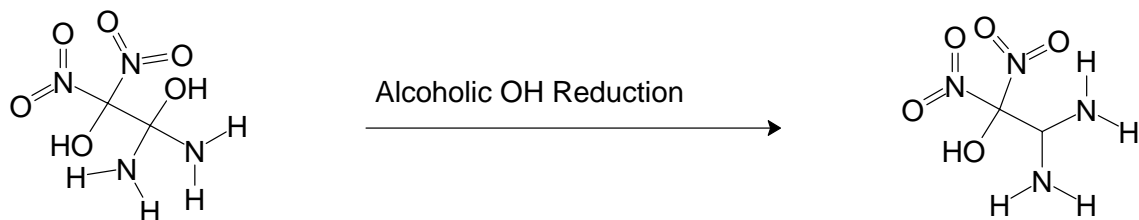

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0,   Bioavailability: 30, Bioaccumulation: 66

Formation of O-Glucuronide II.

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0,   Bioavailability: 30, Bioaccumulation: 60
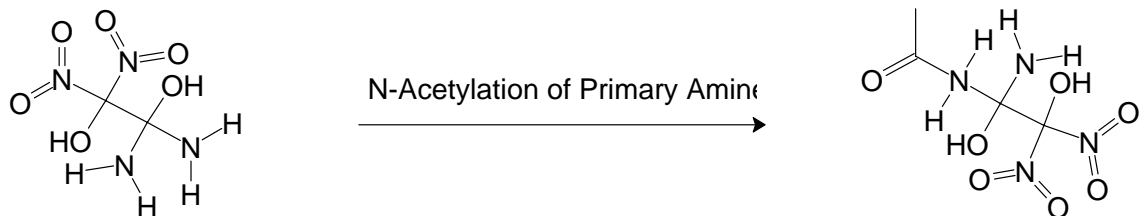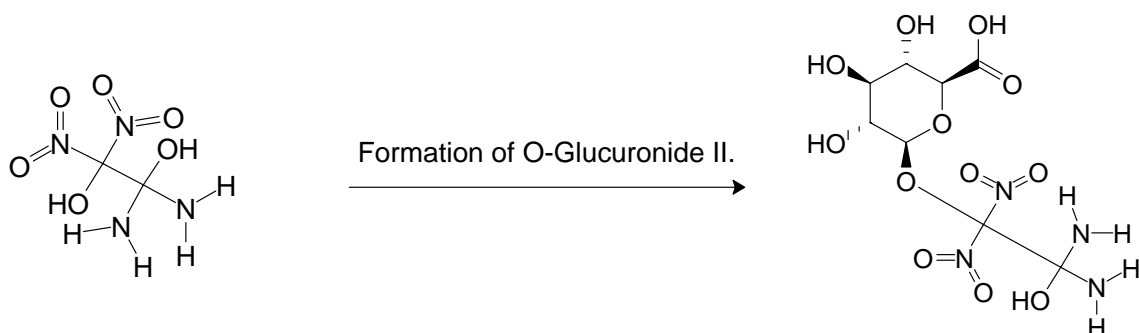
DNNC

No Results for plants, first pass, or animal metabolism.

Photodegradation

Report I

318

Oncogenicity: 82, Mutagenicity: 75, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,   Bioavailability: 40, Bioaccumulation: 66
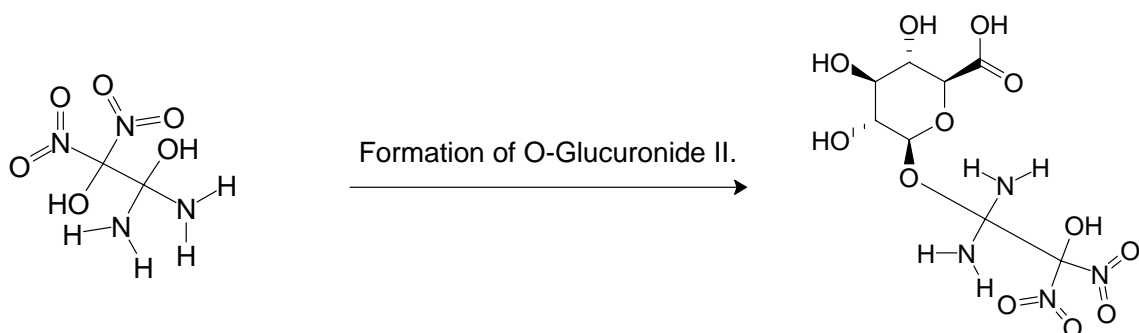
Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 10, Bioaccumulation: 60

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 10, Bioaccumulation: 60

Report II

Oncogenicity: 82, Mutagenicity: 75, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0, Bioavailability: 40, Bioaccumulation: 66

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 10, Bioaccumulation: 60
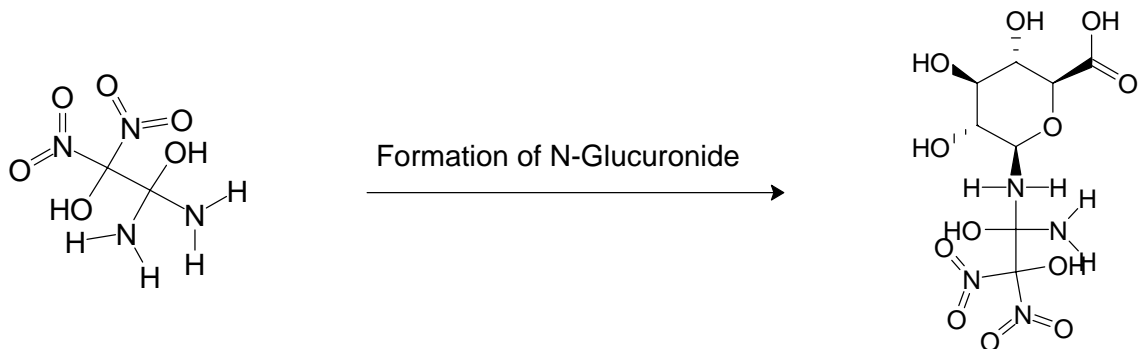
FOX 7

No Results for plants or photodegradation.

First Pass

Report I

Formation of N-Glucuronide

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60
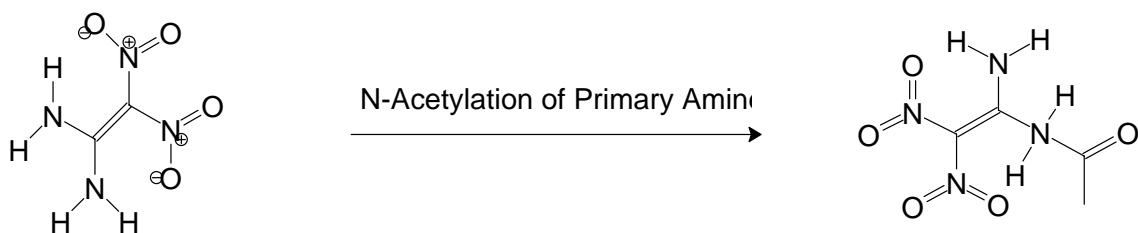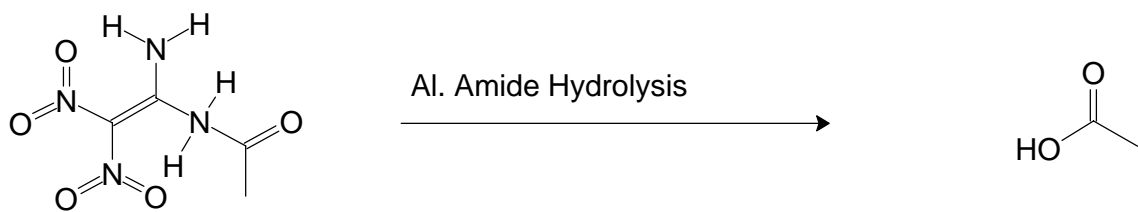

Formation of N-Glucuronide

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60

Animal Metabolism (2 step)

Report I

C=C Double Bond Hydration

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 1, Bioaccumulation: 60
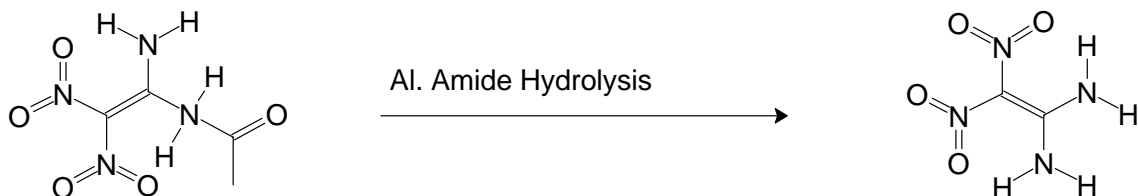

Alcoholic OH Reduction

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 10, Bioaccumulation: 60

N-Acetylation of Primary Amine

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 1, Bioaccumulation: 60

Formation of O-Glucuronide II.

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0,   Bioavailability: 1, Bioaccumulation: 60

Formation of N-Glucuronide

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 1, Bioaccumulation: 60

Report II
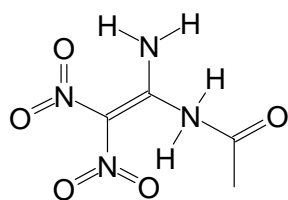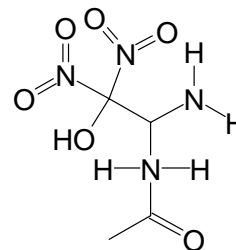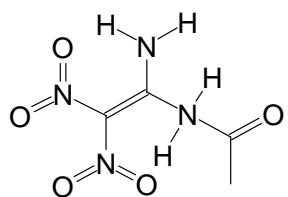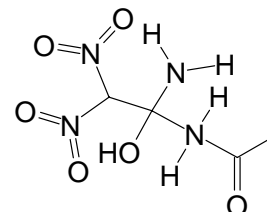

C=C Double Bond Hydration

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 1, Bioaccumulation: 60

Alcoholic OH Reduction

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 10, Bioaccumulation: 60
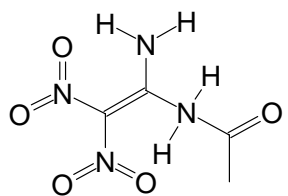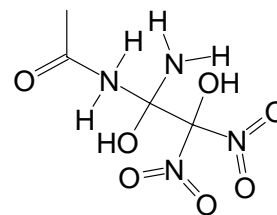

N-Acetylation of Primary Amine

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 1, Bioaccumulation: 60

Formation of O-Glucuronide II.

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0,　　Bioavailability: 1, Bioaccumulation: 60
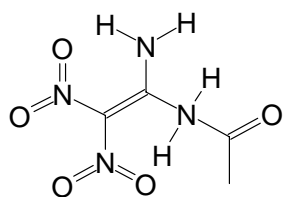

Formation of N-Glucuronide

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 1, Bioaccumulation: 60
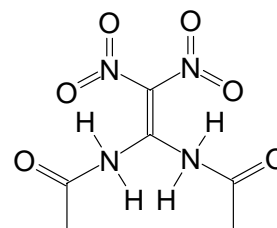
Report III

C=C Double Bond Oxidation

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 5, Bioaccumulation: 60
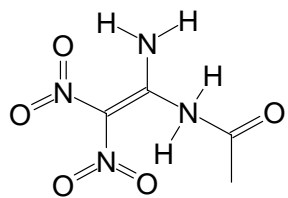

Alcoholic OH Reduction

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 1, Bioaccumulation: 60

Alcoholic OH Reduction

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 1, Bioaccumulation: 60

N-Acetylation of Primary Amine

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 7, Bioaccumulation: 60
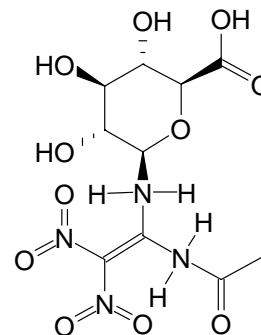

Formation of O-Glucuronide II.

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0,   Bioavailability: 0, Bioaccumulation: 60

Formation of O-Glucuronide II.

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 53, Irritation: 0, Sensitivity: 0, Immunotoxicity: 29, Neurotoxicity: 0,   Bioavailability: 1, Bioaccumulation: 60
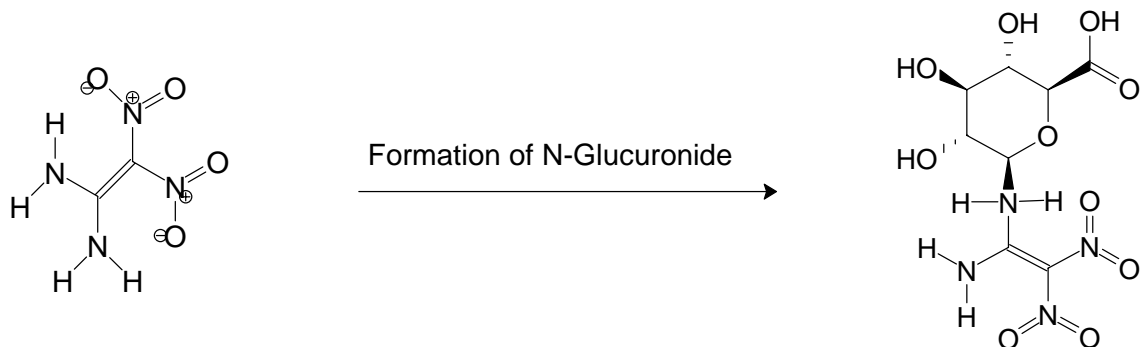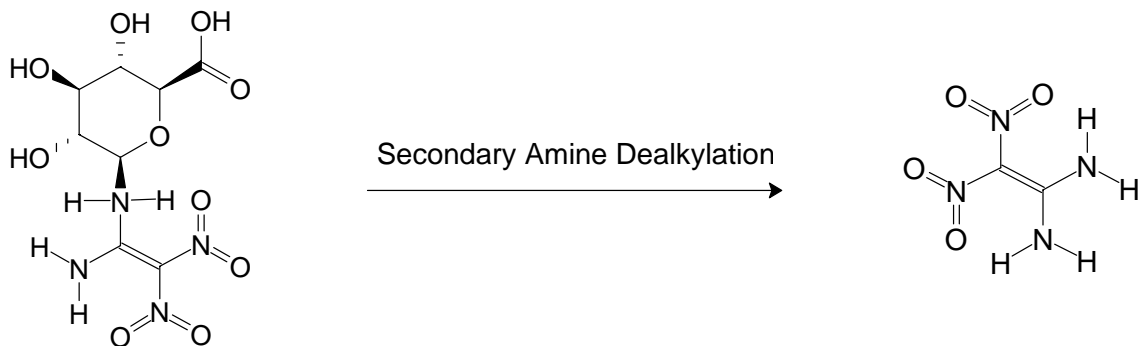
Formation of N-Glucuronide

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60
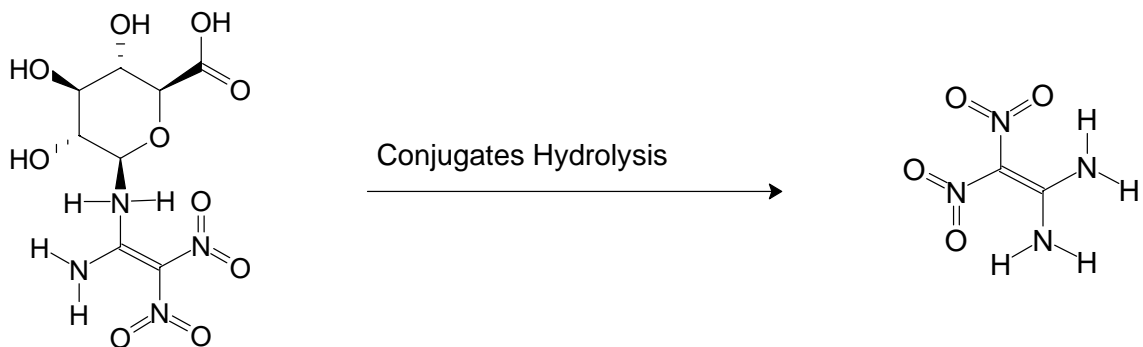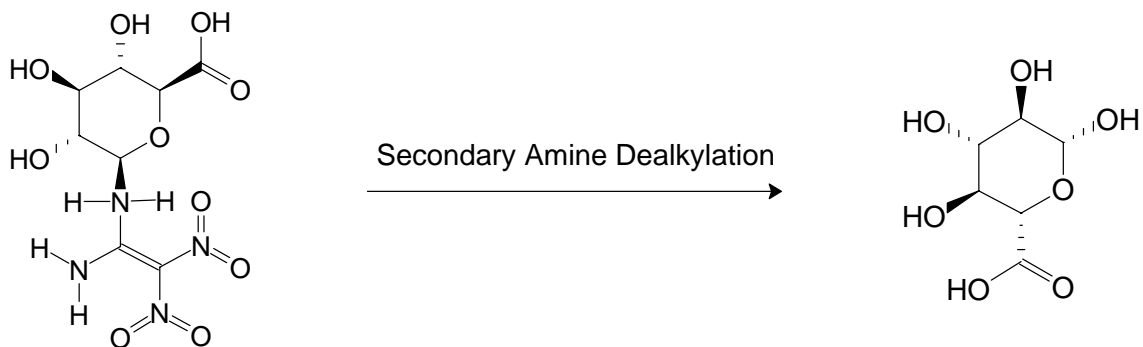
Report IV

N-Acetylation of Primary Amine

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 91

Al. Amide Hydrolysis

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 40, Bioaccumulation: 66
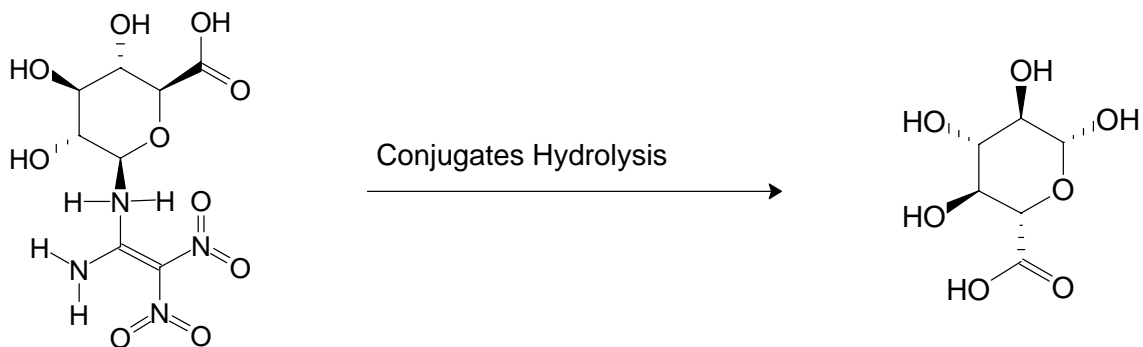

Al. Amide Hydrolysis

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 66
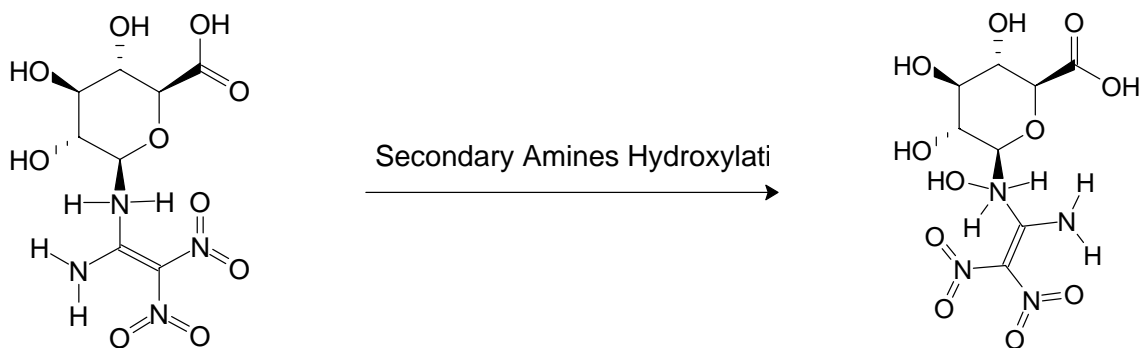
Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 1, Bioaccumulation: 60

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 1, Bioaccumulation: 60

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 7, Bioaccumulation: 60
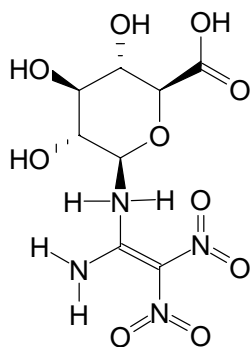

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 66
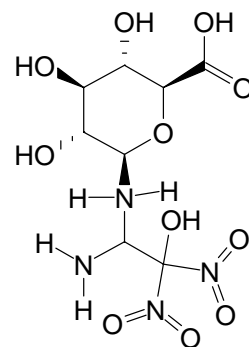
Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60

Report V

Formation of N-Glucuronide
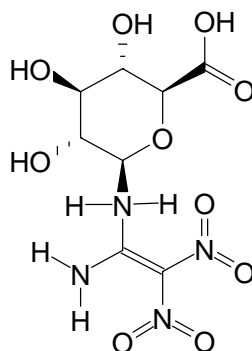
Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60

Secondary Amine Dealkylation

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 66

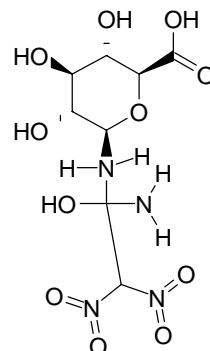
Conjugates Hydrolysis

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 66
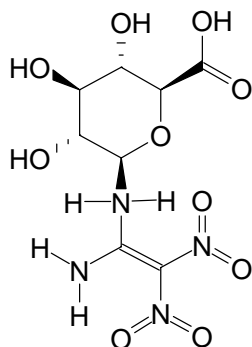
Secondary Amine Dealkylation

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60

Conjugates Hydrolysis

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60

Secondary Amines Hydroxylati

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60
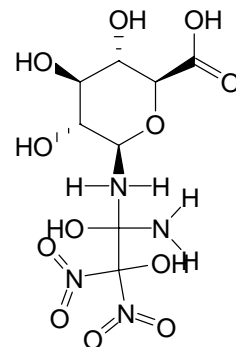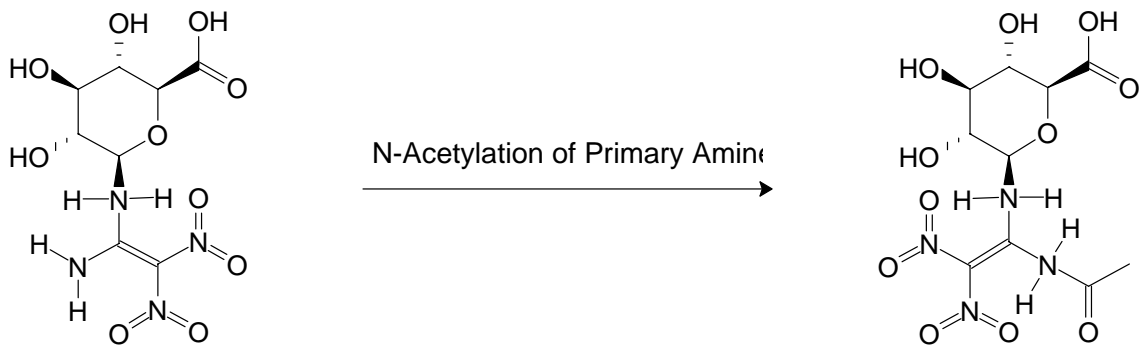
C=C Double Bond Hydration

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 1, Bioaccumulation: 60

C=C Double Bond Hydration

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 1, Bioaccumulation: 60
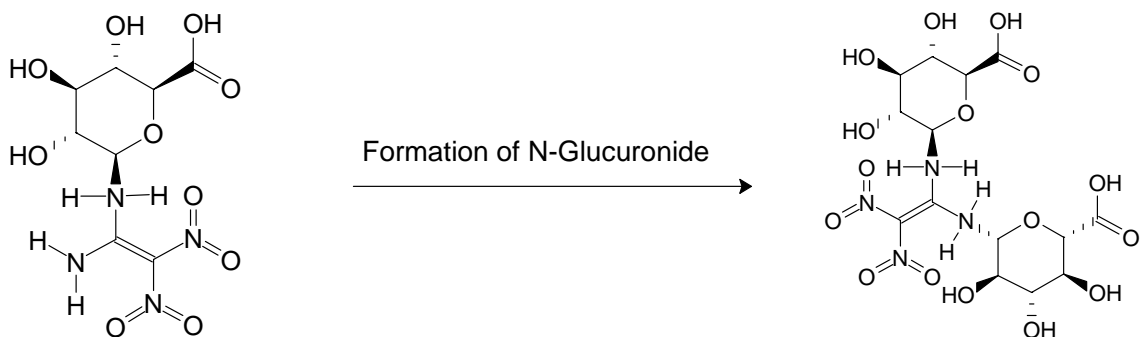

C=C Double Bond Oxidation

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 19, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 0, Bioaccumulation: 60
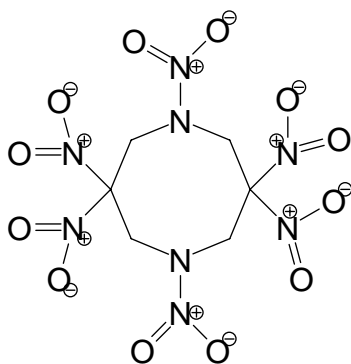
N-Acetylation of Primary Amine

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0, Bioavailability: 0, Bioaccumulation: 60

Formation of N-Glucuronide

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 17, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0, Bioavailability: 0, Bioaccumulation: 60
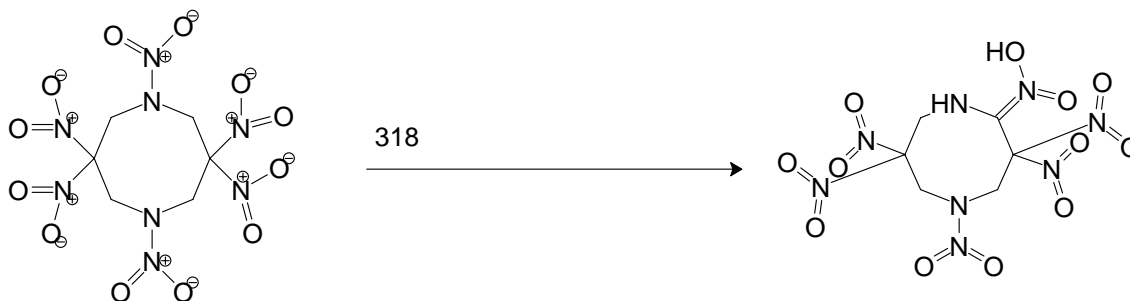
HCO

No Results for plants, first pass, or animal metabolism.

Photodegradation

Report I

318

Oncogenicity: 82, Mutagenicity: 75, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,   Bioavailability: 70, Bioaccumulation: 66
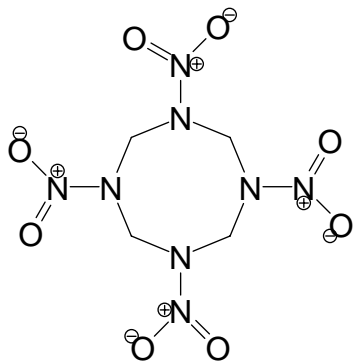

318

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 10, Bioaccumulation: 60

318

Oncogenicity: 0, Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 10, Bioaccumulation: 60

HMX

No Results for plants, first pass, or animal metabolism.

Photodegradation

Report I

Oncogenicity: 82, Mutagenicity: 75, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0, Bioavailability: 100, Bioaccumulation: 91

Oncogenicity: 82, Mutagenicity: 75, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0, Bioavailability: 40, Bioaccumulation: 66

Oncogenicity: 82, Mutagenicity: 75, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0, Bioavailability: 40, Bioaccumulation: 66
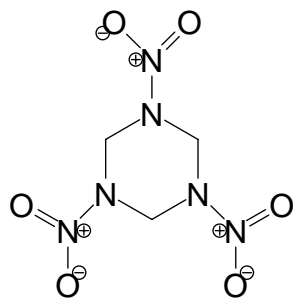
Oncogenicity: 82, Mutagenicity: 75, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0, Bioavailability: 40, Bioaccumulation: 66

Oncogenicity: 82, Mutagenicity: 75, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0, Bioavailability: 40, Bioaccumulation: 66

RDX

No Results for plants, first pass, or animal metabolism.

Photodegradation

Report I

Oncogenicity: 82, Mutagenicity: 75, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0, Bioavailability: 70, Bioaccumulation: 66

Oncogenicity: 82, Mutagenicity: 75, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0, Bioavailability: 10, Bioaccumulation: 60

Oncogenicity: 0 Mutagenicity: 0, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0,Bioavailability: 10, Bioaccumulation: 60

Oncogenicity: 82, Mutagenicity: 75, Teratogenicity: 0, Irritation: 0, Sensitivity: 0, Immunotoxicity: 0, Neurotoxicity: 0, Bioavailability: 10, Bioaccumulation: 60

8.3   LIST OF TECHNICAL PUBLICATIONS

Predictive Methods for Environmental Screening of Proposed Perchlorate Replacements
JANNAF 33rd Propellant & Explosives Characterization and Development Subcommittee &
22nd Safety & Environmental Protection Subcommittee, March 6-9, 2006